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The Study of Ion–Molecule Reactions in Chloroethylene by Ion Cyclotron Resonance Spectroscopy

J. L. Beauchamp,[1] L. R. Anders, and J. D. Baldeschwieler

Contribution from the Department of Chemistry, Stanford University, Stanford, California. Received February 6, 1967

Abstract: Bimolecular ion–molecule reactions in chloroethylene have been studied using ion cyclotron single- and multiple-resonance techniques. Consecutive reactions are followed to a high order at low pressure by appropriate ion-trapping conditions. The most general reaction observed is of the type $A^+ + C_2H_3Cl \rightarrow AC_2H_2^+ + HCl$. The reaction of $C_2H_3Cl^+$ with C_2H_3Cl yields three products: $C_3H_4Cl^+$, $C_4H_5Cl^+$, and $C_4H_6Cl^+$. In all three cases the chlorine in the product comes with equal probability from the charged or neutral reactant.

I. Introduction

The collision of an ion with a neutral molecule at low pressures can give rise to a generalized bimolecular reaction of the type

$$A^+ + B \longrightarrow C^+ + D \qquad (1)$$

Reactions of this type frequently involve the formation of a chemically interesting intermediate species which rapidly fragments in the absence of a stabilizing collision. The nature of the intermediate species and the fragments into which it decomposes have become a popular subject for theoretical and experimental analysis.[2] For example, the phase space theory of chemical kinetics developed by Light[3] and his-co-workers appears to give an adequate description of three-body ion–molecule reactions, and will undoubtedly be extended with approximations to predict the decomposition of larger intermediate complexes. The experimental techniques available for the study of ion–molecule reactions have been reviewed by various authors,[2] and recent interest has been sufficient to warrant the publication of a monograph on the subject.[4] Tandem mass spectrometers, for example, provide a wealth of data on various aspects of primary ion–molecule reactions.[5,6] However the available techniques have not been particularly suitable for the study of complex, high-order ion–molecule reaction sequences. Ion cyclotron resonance provides a straightforward method which uniquely fulfills this need.

Ion cyclotron resonance spectroscopy (icr) is based on the classical motion of charged particles in magnetic and electric fields. The motion of a free charged particle in a uniform magnetic field is constrained to a circular orbit of angular frequency ω_c in a plane normal to H, and is unrestricted parallel to H. The cyclotron frequency, ω_c, is independent of velocity and is given in gaussian cgs units by

$$\omega_c = eH/mc \qquad (2)$$

where e is the charge of the particle, H the magnetic field strength, m the particle mass, and c the speed of light. The radius of the circular motion is given by

$$r = v_\perp/\omega_c \qquad (3)$$

where $v_\perp$ is the component of ion velocity in the plane

(1) National Science Foundation Predoctoral Fellow, on Traveling Guidance from Harvard University.

(2) (a) F. W. Lampe, J. L. Franklin, and F. H. Field, *Progr. Reaction Kinetics*, **1**, 68 (1961); (b) C. F. Giese, *Advan. Chem. Phys.*, **10**, 247 (1966).

(3) J. Lin and J. Light, *J. Chem. Phys.*, **45**, 2545 (1966).

(4) "Ion-Molecule Reactions in the Gas Phase," Advances in Chemistry Series, No. 58, American Chemical Society, Washington, D. C., 1966.

(5) E. Lindholm, ref 4, Chapter 1.

(6) L. W. Sieck, F. P. Abramson, and J. H. Futrell, *J. Chem. Phys.*, **45**, 2859 (1966).
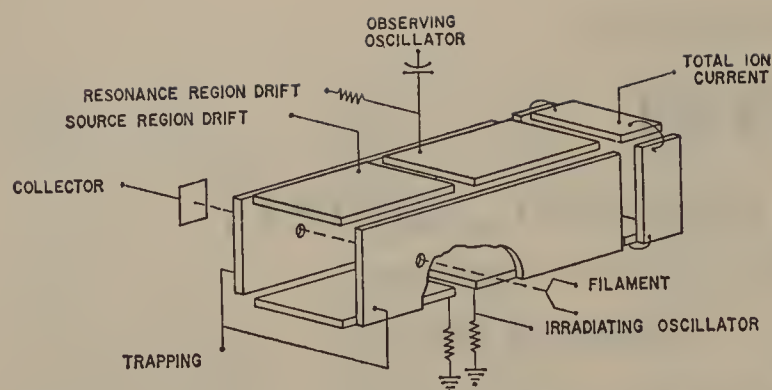
Figure 1. Cutaway view of cyclotron resonance cell. The electron beam is collinear with the magnetic field.

Figure 2. Block diagram of cyclotron resonance apparatus.

perpendicular to the field direction. Typical values for these parameters are, in the case of argon ions at thermal energies in an 8-kgauss field, $\omega_c = 307$ kc/sec and $r = 0.02$ cm. When an alternating electric field, $E_1(t)$ at frequency ω_1, is applied normal to H with $\omega_1 = \omega_c$, an absorption of energy by the ions occurs which can be readily observed using a marginal oscillator–detector. With a fixed observing frequency, a spectrum linear in mass can be obtained by sweeping the magnetic field.

In an ionized gas at a pressure where a reaction of the type 1 occurs, both C^+ and A^+ can be detected by the observing oscillator–detector. A second alternating electric field, $E_2(t)$ at frequency ω_2, applied at the cyclotron frequency of A^+ can cause a significant change in the rate of reaction 1 by heating the reactant ion. This results in an easily detectable change in the measured absorption of energy by the product C^+ from $E_1(t)$. This double-resonance technique has been successfully applied to the study of charge exchange among isotopes of the rare gases[7] and to the reaction[8]

$$CD_4^+ + N_2 \longrightarrow N_2D^+ + CD_3 \qquad (4)$$
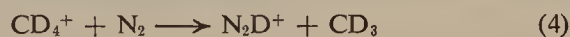
for which an increase in the N_2D^+ absorption was effected by irradiating CD_4^+. Ion cyclotron multiple resonance thus provides a simple means of identifying reactant ions in a reaction mixture, even in the presence of competing processes.

This paper illustrates the application of cyclotron resonance techniques to the study of ion–molecule reactions in chloroethylene. The apparatus and experimental conditions are described in detail in section II. The rather complex scheme of sequential ion–molecule reactions occuring in chloroethylene is analyzed in section III, with the significance of some of the reactions of interest being considered in detail in section IV.

II. Experimental Section

The basic ion cyclotron resonance spectrometer utilized in these experiments was constructed by Varian Associates.[9] As this is the first report of an extensive study of ion chemistry employing cyclotron resonance techniques, a complete description of the apparatus is given.

A cutaway view of the cyclotron resonance cell is shown in Figure 1. The cell is divided equally into a source and resonance region with over-all dimensions of $2.54 \times 2.54 \times 12.7$ cm. Electrons from a rhenium filament are accelerated in the direction of the magnetic field by a negative bias on the filament and enter the
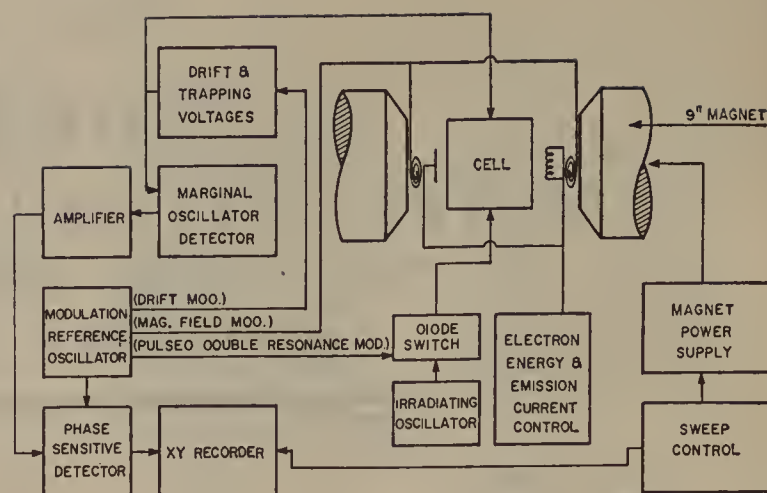
source region of the resonance cell through the side plate. The electron beam traverses the source region and is measured on a collector biased at +20 v with respect to the resonance cell. The emission current is operated between 0.1 and 10 μa and is regulated to maintain a constant value as the magnetic field is swept. Trapping voltages applied to the side plates constrain the ion motion in the direction of the magnetic field. Ions are drifted from the source into the resonance regions by the application of static voltages to the top plates of the cell. The drift velocity in the crossed field geometry is in a direction perpendicular to both the magnetic and static electric fields with a magnitude given by[10]

$$v_d = \frac{cE_s}{H} \qquad (5)$$

where E_s is the static electric field strength. Since v_d is independent of charge, both negative and positive ions move in the same direction. With typical values for H and E_s of 5 kgauss and 0.25 v/cm, respectively, $v_d = 5.0 \times 10^3$ cm/sec. Separation of positive and negative ions is effected by selecting the appropriate sign for the trapping voltage. Separate drift voltages are applied to the resonance and source regions to isolate the observing oscillator from the source region and the effects of the electron beam. The top and bottom plates of the resonance region form part of the capacitance in the tank circuit of a marginal oscillator. The marginal oscillator is chosen for its high sensitivity in detecting small impedance changes[11] in the tank circuit. The irradiating oscillator is usually operated at a level above that of the observing oscillator. The simple method of coupling the irradiating voltage to the resonance cell shown in Figure 1 provides adequate decoupling of the irradiating and detecting circuits.

A block diagram of the apparatus is given in Figure 2. The resonance cell is placed between the pole caps of a Varian Associates 9-in. electromagnet with a 1.75-in. gap. The output of the marginal oscillator–detector is amplified and fed to a phase-sensitive detector. The phase-sensitive detector is referenced to a modulation oscillator which provides the three modulation options shown in Figure 2. The first scheme involves modulation of the magnetic field with Helmholtz coils located on the pole caps. The field-modulation method operates in the same fashion as it does when applied to nuclear magnetic resonance and electron paramagnetic resonance.[12] The level of the modulation is adjusted below the point where distortion of the line shape occurs. The spectra thus obtained are insensitive to the ion distribution in the resonance probe. Figures 3 and 4 display typical field-modulation spectra with the characteristic derivative line shapes.

The second of these schemes involves modulation of the drift voltages. This causes a variation in the ion transit time and thereby provides a modulation of the ion number density in the cell. The resulting absorption spectra are as shown in Figure 5. The phase of the signal arising from drift modulation is very sensitive to the ion distribution along the length of the cell. At low pressure the distribution is uniform. This uniformity is disrupted by reactions

(7) L. R. Anders, J. L. Beauchamp and J. D. Baldeschwieler, *J. Chem. Phys.*, in press.

(8) L. R. Anders, J. L. Beauchamp, R. C. Dunbar, and J. D. Baldeschwieler, *ibid.*, 45, 1062 (1966).

(9) Syroton mass spectrometer, Varian Associates, Palo Alto, Calif.

(10) J. D. Jackson, "Classical Electrodynamics," John Wiley and Sons, Inc., New York, N. Y., 1962, p 412.

(11) F. N. H. Robinson, *J. Sci. Instr.*, 36, 481 (1959).

(12) "NMR and EPR Spectroscopy," Pergamon Press, New York, N. Y., 1960, Chapter 14.
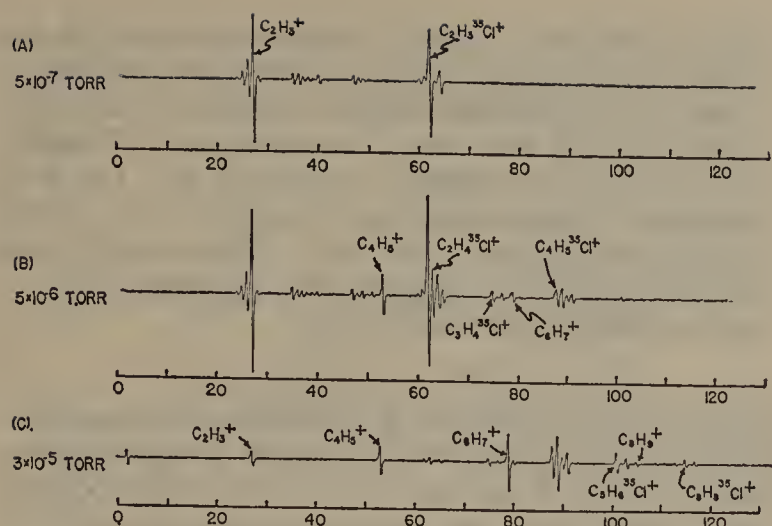
Figure 3. Variation of single-resonance 70-ev electron energy chloroethylene spectra with pressure. For all three spectra $\omega_1 = 153.0$ kc and $E_1 = 0.01$ v/cm. Field modulation gives the derivative line shape. The most probable ionic species corresponding to a number of peaks are given for reference.
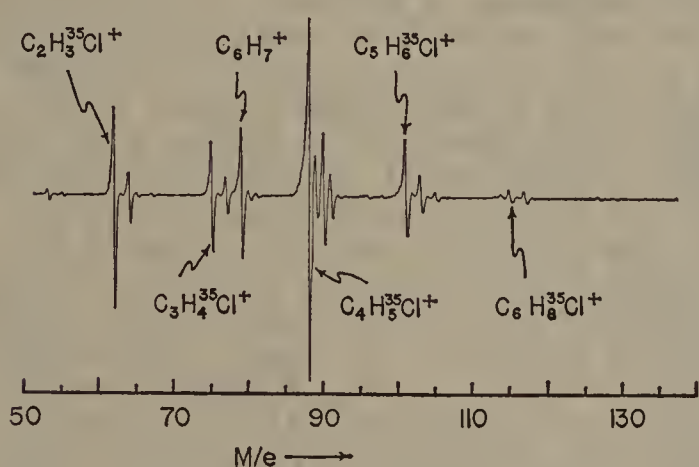
Figure 4. Single-resonance spectrum of chloroethylene with 11-ev electron energy at 3×10^{-6} torr pressure. No major peaks were recorded below m/e 50. The most probable ionic species corresponding to a number of peaks are given for reference.

Figure 5. Single-resonance spectrum of chloroethylene with 70-ev electron energy at 4×10^{-4} torr. Drift voltage modulation gives the absorption line shape. No peaks were recorded above m/e 50.

Figure 6. Pulsed double-resonance spectrum of the m/e 53 ($C_4H_5^+$) species with irradiation at the cyclotron frequency of $C_2H_3^+$. The irradiating power in spectrum B is increased 5 db over that used in spectrum A. The sharp feature at m/e $26\frac{1}{2}$ is due to the irradiating oscillator exciting the first overtone of the marginal oscillator.

which occur at higher pressure, the density of reaction products increasing with the distance from the electron beam. Since the reactant density is higher at the entrance to the resonance region, it is not difficult to obtain drift modulation spectra in which the reactant and product peaks are inverted with respect to each other. This situation is not desirable if meaningful intensity measurements are to be made.

The third modulation scheme is an integral part of the highly specific double-resonance technique for identifying ion–molecule reactions. The reference oscillator operates a diode switch which permits square-wave modulation of the irradiating oscillator. The rate of an ion–molecule reaction usually shows *at least* a slight variation with ion energy causing a *change* in number density of product ions when the irradiating oscillator is switched off and on. The modulation information necessary for the marginal oscillator and phase-sensitive detector to produce a signal is thus transmitted only through an ion–molecule reaction. The over-all detection scheme effectively displays the difference between the product ion absorption spectrum with and without reactant irradiation. Figure 6 shows typical pulsed double resonance spectra obtained with frequency sweep of the irradiating oscillator at fixed magnetic field. The dependence of the pulsed double-resonance line shape on the irradiating power has been considered in detail for charge-transfer reactions in mixtures of rare gas isotopes, and bears an interesting analogy to the effects of chemical exchange on nmr and esr line shapes.[7] The modulation frequency employed in all three schemes is $\sim$40 cps.

The resonance probe is contained in a bakeable stainless steel high-vacuum system which can be evacuated to below 10^{-8} torr with an 8-l./sec ion pump. The sample to be studied is admitted through a variable leak valve from a reservoir at 20 torr. All of the spectra discussed were obtained under dynamic conditions with
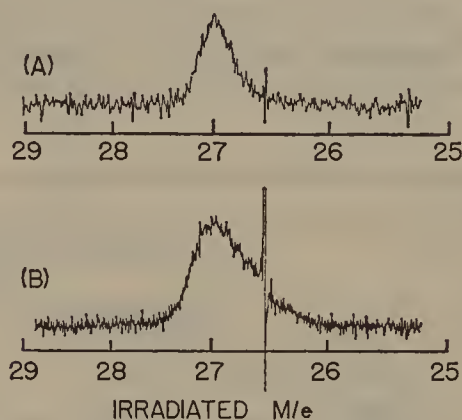
the desired pressure being maintained by varying the leak rate and pumping speed. This prevents accumulation of impurity gases in the system and permits operation of the spectrometer between 10^{-8} and 10^{-2} torr. Pressure measurements were made with an ionization gauge. Since means for accurately calibrating the gauge for chloroethylene in the pressure range employed were not available, the absolute values are probably reliable only to within an order of magnitude.

The chloroethylene (99.9% purity) and methane (ultrahigh purity grade, 99.95% purity) were obtained from Matheson and used without further purification. The perdeuteriomethane was obtained from Merck Sharp and Dohme of Canada.

III. Results

A. Variation of Single Resonance Spectra with Pressure. Figure 3 shows the appearance of the single-resonance icr spectra of chloroethylene obtained from 70-ev electrons at three different pressures with drift voltages set to approximately 1 v. The observing oscillator is operated at 153 kc/sec with $\sim$0.01-v/cm radiofrequency level. Magnetic field modulation gives the derivative line shape. At 5×10^{-7} torr (Figure 3A) no reactions are observed, and the resulting spectrum corresponds closely to that obtained using a conventional mass spectrometer.[13] The only significant difference between the icr and conventional mass spectra at low pressure is the value of 4.8:1 obtained for the $^{35}Cl/^{37}Cl$ ratio in the parent ion in contrast with the expected value of 3:1.[13] No impurities other than a trace of argon at m/e 40 are evident.

At 5×10^{-6} torr (Figure 3B) numerous reaction products appear in the icr spectrum. The two chlorine isotopes serve as an aid in the identification of chlorine-containing reaction products. Analysis of the spectrum in Figure 3B indicates that the majority of the reac-

(13) "Mass Spectral Data," Manufacturing Chemists Association Research Project, Serial No. 122.

tion products are separated from parent ions by 26 mass units. This corresponds to the incorporation of a C_2H_2 group in the parent ion and suggests the general reaction

$$A^+ + C_2H_3Cl \longrightarrow AC_2H_2^+ + HCl \qquad (6)$$

where A^+ is any of a number of ionic species present in the system. Figure 3C shows the chloroethylene mass spectrum at 3×10^{-5} torr. At this pressure the product ion intensity exceeds that of the parent ions.

All the observed m/e values and most likely ionic species to which they correspond are given in Tables I and II. The relative intensities of the major species at higher pressure are evident in Figure 3B and C.

Table I. Summary of Observed Ionic Species Appearing at Low Pressure

| | | Relative intensity | |
| | | Icr spectrum[b] | Conventional mass |
m/e	Species[a]	$(5 \times 10^{-7}$ torr)	spectrometer[c]
24	C_2^+	2.6	3.95
25	C_2H^+	10.4	13.78
26	$C_2H_2^+$	28.7	34.0
27	$C_2H_3^+$	100.0	100.0
35	$^{35}Cl^+$	6.8	8.76
36	$H^{35}Cl^+$	6.5	1.98
37	$^{37}Cl^+$	2.4	2.83
38	$H^{37}Cl^+$	2.1	0.65
47	$C^{35}Cl^+$	5.0	4.23
48	$CH^{35}Cl^+$	2.7	1.77
49	$C^{37}Cl^+$	1.6	1.48
50	$CH^{37}Cl^+$	0.9	0.63
59	$C_2^{35}Cl^+$	0.9	1.42
60	$C_2H^{35}Cl^+$	4.1	4.62
61	$C_2H_2^{35}Cl^+$, $C_2^{37}Cl^+$	7.4	6.87
62	$C_2H_3^{35}Cl^+$, $C_2H^{37}Cl^+$	84.8	76.6
63	$C_2H_2^{37}Cl^+$	3.0	3.80
64	$C_2H_3^{37}Cl^+$	17.7	24.2

[a] Contributions attributed to ^{13}C isotope neglected. [b] Data taken from spectrum shown in Figure 3A. [c] "Mass Spectral Data," Manufacturing Chemists Association Research Project, Serial No. 122. Instrument: Consolidated No. 21-103 mass spectrometer.

Table II. Summary of Observed Ionic Species Appearing at High Pressure

m/e	Species	m/e	Species
2	H_2^+	89	$C_4H_6^{35}Cl^+$
3	H_3^+	90	$C_4H_5^{37}Cl^+$
12	C^+	91	$C_4H_6^{37}Cl^+$, $C_7H_7^+$
16	CH_4^+	101	$C_5H_6^{35}Cl^+$
28	$C_2H_4^+$, CO^+	103	$C_5H_6^{37}Cl^+$
29	$C_2H_5^+$, COH^+	105	$C_8H_9^+$
39	$C_3H_3^+$	109	$C_3H_3^{35}Cl^{35}Cl^+$
53	$C_4H_5^+$	111	$C_3H_3^{35}Cl^{37}Cl^+$
63	$C_2H_4^{35}Cl^+$	113	$C_3H_3^{37}Cl^{37}Cl^+$
65	$C_2H_4^{37}Cl^+$, $C_5H_5^+$	114	$C_6H_7^{35}Cl^+$
73	$C_3H_2^{35}Cl^+$	115	$C_6H_8^{35}Cl^+$
75	$C_3H_4^{35}Cl^+$	116	$C_6H_7^{37}Cl^+$
77	$C_3H_4^{37}Cl^+$	117	$C_6H_8^{37}Cl^+$
79	$C_6H_7^+$	125	(?)
83	$CH^{35}Cl^{35}Cl^+$	127	$C_7H_8^{35}Cl^+$
85	$CH^{35}Cl^{37}Cl^+$	129	$C_7H_8^{37}Cl^+$
87	$CH^{37}Cl^{37}Cl^+$		
88	$C_4H_5^{35}Cl^+$		

At 11-ev electron energy no fragmentation occurs and only the parent ion is observed. As the pressure is

raised it becomes possible to observe reactions of the parent ion exclusively. Figure 4 shows the appearance of the single-resonance spectrum obtained with 11-ev electrons at 3×10^{-6} torr. No mass peaks of significant intensity were observed below m/e 50. The drift voltages are again set to approximately 1 v in the source and resonance regions of the cell. The absence of the $C_2H_4Cl^+$ peak at 11 ev suggests that its mode of formation involves $C_2H_3^+$ in the reaction

$$C_2H_3^+ + C_2H_3Cl \longrightarrow C_2H_4Cl^+ + C_2H_2 \qquad (7)$$

The other peaks in Figure 4 relate closely to those observed at 70 ev. The ^{35}Cl:^{37}Cl ratio observed in the parent ion with 11-ev electrons is 4.2:1. At 4×10^{-4} torr the only major peaks in the low mass region occur at m/e 12, 16, and 29 as shown in Figure 5. The resonances could correspond to C^+, CH_4^+, and $C_2H_5^+$ or HCO^+. No other peaks were observed up to m/e 130. Above 4×10^{-4} torr the spectra become appreciably collision broadened[14] and the mass resolution is poor.

B. Identification of Reactions. The two reactions 6 and 7 were inferred by the usual techniques[2] of varying pressure and electron energy. It is evident in Figure 4 that a fairly complex sequence of reactions occurs starting simply with the addition of the parent ion to the parent neutral. The application of double-resonance techniques directly demonstrates whether or not suspected reactions occur. In the pulsed double-resonance scheme the intensity of the product peak is monitored while the pulsed irradiating field is swept. Figure 6 demonstrates the pulsed double-resonance spectrum of the m/e 53 peak. A change is noted when the m/e 27 peak is irradiated. As the irradiating power is increased from Figure 6A to Figure 6B by a factor of 5 db, the width of the pulsed double-resonance spectrum increases from 0.3 to 0.6 mass unit, corresponding to an increased heating of the reactant ion. The sharp feature at m/e $26\frac{1}{2}$ corresponds to the spurious excitation of the first overtone of the marginal oscillator–detector by the irradiating oscillator.

The reaction thus identified is the first of the sequence

$$C_2H_3^+ + C_2H_3Cl \longrightarrow C_4H_5^+ + HCl \qquad (8a)$$
$$C_4H_5^+ + C_2H_3Cl \longrightarrow C_6H_7^+ + HCl \qquad (8b)$$
$$C_6H_7^+ + C_2H_3Cl \longrightarrow C_8H_9^+ + HCl \qquad (8c)$$

in which all reactions are of the general type (6) and have been confirmed by double resonance. This sequence is of course also eliminated if 11-ev electrons are used. Reaction 8b is, however, only one of the reactions yielding the species $C_6H_7^+$. At higher pressures the $C_8H_9^+$ species exhibits only a small fraction of the intensity attained at intermediate pressures by $C_4H_5^+$ or $C_6H_7^+$. Double resonance also confirms reaction 7 which is followed by the sequence

$$C_2H_4Cl^+ + C_2H_3Cl \longrightarrow C_4H_6Cl^+ + HCl \qquad (9a)$$
$$C_4H_6Cl^+ + C_2H_3Cl \longrightarrow C_6H_8Cl^+ + HCl \qquad (9b)$$

where again the reactions are of type 6. The mass pattern between m/e 62 and 65 is repeated 26 mass units higher. This is shown clearly in Figure 7A. Figure 7B shows the pulsed double-resonance spectrum resulting from sweeping the magnetic field with $\omega_1/\omega_2 = 62/88$. Thus when the ion of m/e 88 is being observed, the ion of m/e 62 is being irradiated. This permits ob-

(14) J. L. Beauchamp, *J. Chem. Phys.*, **46**, 1231 (1967).
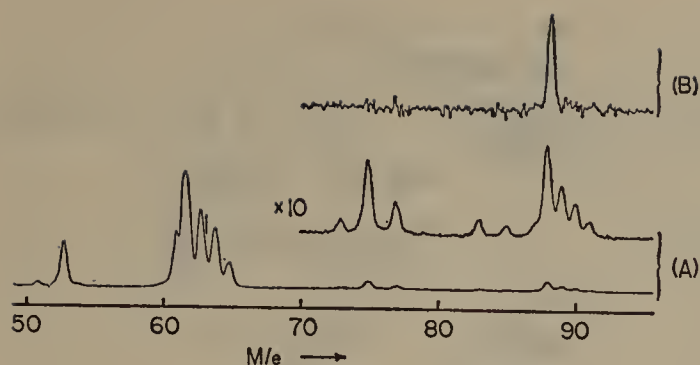
Figure 7. (A) Field-sweep single-resonance spectrum of chloro-ethylene with 70-ev electron energy at 5×10^{-6} torr. Drift voltage modulation gives the absorption line shape. (B) Field-sweep pulsed double-resonance spectrum. ω_1/ω_2 is fixed in the ratio 62/88.

Figure 8. Pulsed double-resonance spectra showing the relative contributions of the parent chlorine isotopes to the product chlorine isotopes for $C_3H_4Cl^+$ and $C_4H_5Cl^+$ at 3×10^{-6} torr and 11-ev electron energy.

servation of the reaction

$$C_2H_3{}^{35}Cl^+ + C_2H_3Cl \longrightarrow C_4H_5{}^{35}Cl^+ + HCl \qquad (10)$$

and gives the single peak in Figure 7B. The resolution with drift modulation is not as good as that obtained with field modulation.

The reactions of the parent ion are best examined with 11-ev electron energy where no fragments other than the parent ion are formed. It is of interest to extend the identification of reaction 10 to examine the origin of the chlorine retained in the product ion. The resonances of the ^{35}Cl- and ^{37}Cl-containing species of both the reactant and product ions are well resolved. Thus it is possible to observe the ^{37}Cl-containing product with irradiation of the ^{35}Cl and ^{37}Cl reactants, or to observe the ^{35}Cl-containing product with irradiation of the ^{35}Cl- and ^{37}Cl-containing reactants. The relative intensities of these double-resonance spectra will depend in a simple way (as discussed in section IV) on the probability that the Cl atom from either the ionized or neutral reactant is retained in the product ion. Figure 8C displays the pulsed double-resonance spectrum of $C_4H_5{}^{37}Cl^+$. It is apparent that both $C_2H_3{}^{35}Cl^+$ and $C_2H_3{}^{37}Cl^+$ contribute to the product containing the ^{37}Cl isotope. Figure 8D displays the relative contribution of the parent ions to $C_4H_5{}^{35}Cl^+$. Similar behavior is observed in the reaction

$$C_2H_3Cl^+ + C_2H_3Cl \longrightarrow C_3H_4Cl^+ + CH_2Cl \qquad (11)$$

where the results of observing $C_3H_4{}^{37}Cl^+$ and $C_3H_4{}^{35}Cl^+$ while irradiating the parent ions are shown in Figures 8A and B, respectively. For both reactions 10 and 11 the Cl atom in the product comes with equal probability from the charged or neutral reactant (section IV).

The peaks corresponding to $C_4H_6{}^{35}Cl^+$ (m/e 89) and $C_4H_6{}^{37}Cl^+$ (m/e 91) come primarily from $C_2H_4Cl^+$ at 70 ev via reaction 9a. At 11 ev no $C_2H_4Cl^+$ is formed, and the intensity of $C_4H_6Cl^+$ is diminished as shown in Figure 4 but does not entirely disappear. Figures 9A and B show respectively the pulsed double-resonance spectra for the m/e 89 and 91 ions at 11 ev and 70 ev under conditions such that only the principal secondary reactions are observed (Figure 3B). At 11 ev only the reaction

$$C_2H_3Cl^+ + C_2H_3Cl \longrightarrow C_4H_6Cl^+ + Cl \qquad (12)$$

is observed. At 70 ev the double-resonance contributions from reaction 9a are also evident. At 11 ev and under conditions such that high order reactions are ob-

served (Figure 4) the pulsed double-resonance spectrum of the m/e 91 ion (Figure 9C) is not nearly so straightforward; m/e 91 corresponds to $C_4H_6{}^{37}Cl^+$ and $C_7H_7{}^+$. The relative intensities of the m/e 89 and 91 peaks suggest that of the two ions with m/e 91, $C_7H_7{}^+$ makes a major contribution to the observed intensity. The pulsed double-resonance spectrum in Figure 9C shows a large contribution to m/e 91 from m/e 65. The m/e 65 ion, evident as a small peak in the single resonance spectrum of Figure 4, is quite reasonably $C_5H_5{}^+$ with the resulting reaction to give m/e 91 being
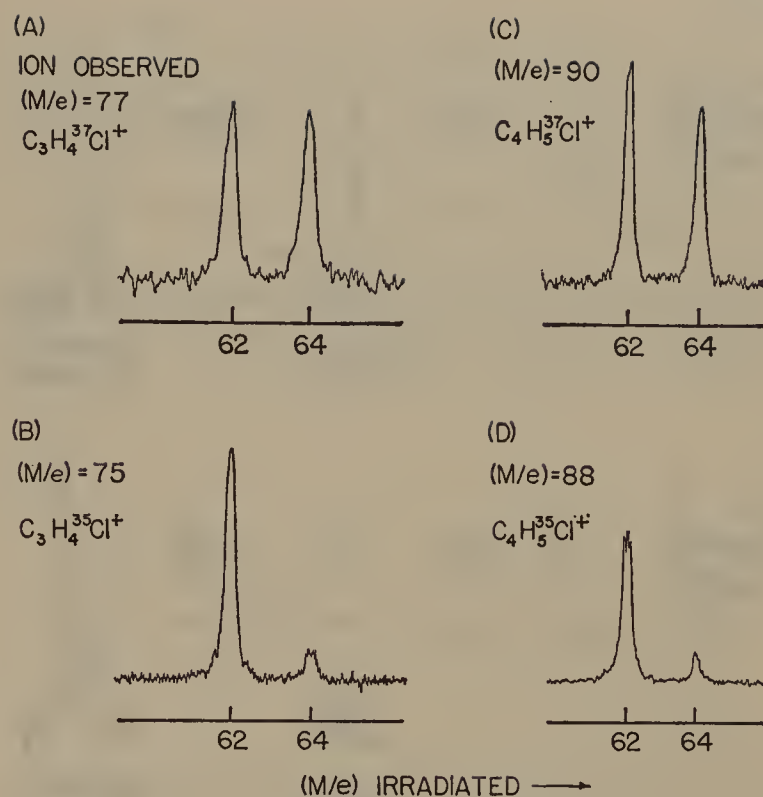
$$C_5H_5{}^+ + C_2H_3Cl \longrightarrow C_7H_7{}^+ + HCl \qquad (13)$$
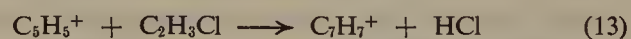
The m/e 65 to 75 relative intensity in the double-resonance spectrum shown in Figure 9C is much greater than the 65 to 75 intensity ratio in the single resonance spectrum of Figure 4. This suggests that although reaction 13 couples m/e 65 to m/e 91 in one step, the other observed contributions proceed to $C_7H_7{}^+$ through at least two or more successive reactions. $C_3H_4Cl^+$, for instance, must undergo a minimum of two reactions to form $C_7H_7{}^+$.

Figure 10 shows the relative contributions of the parent chlorine isotopes to the product ion isotopes in the reaction

$$C_3H_4Cl^+ + C_2H_3Cl \longrightarrow C_5H_6Cl^+ + HCl \qquad (14)$$

The relative contributions of the parent chlorine isotopes to the product are similar to those observed in the two products examined in Figure 8. Table III summarizes the relative contributions of the parent isotopes to the product isotopes in the five reactions considered above which involve a single chlorine in both the parent and product ions.

Other reactions which have been observed and verified by double resonance include (at 70 ev)

$$CCl^+ + C_2H_3Cl \longrightarrow CHCl_2{}^+ + C_2H_2 \qquad (15)$$

(A)
(M/e)=89
$C_4H_6{}^{35}Cl^+$

11 ev   70 ev

60 65   60 65

(B)
(M/e)=91
$C_4H_6{}^{37}Cl^+$

11 ev   70 ev

60 65   60 65

(C)
(M/e)= 91
$C_4H_6{}^{37}Cl^+$
&
$C_7H_7^+$

60   70   80   90

(M/e) IRRADIATED ⟶
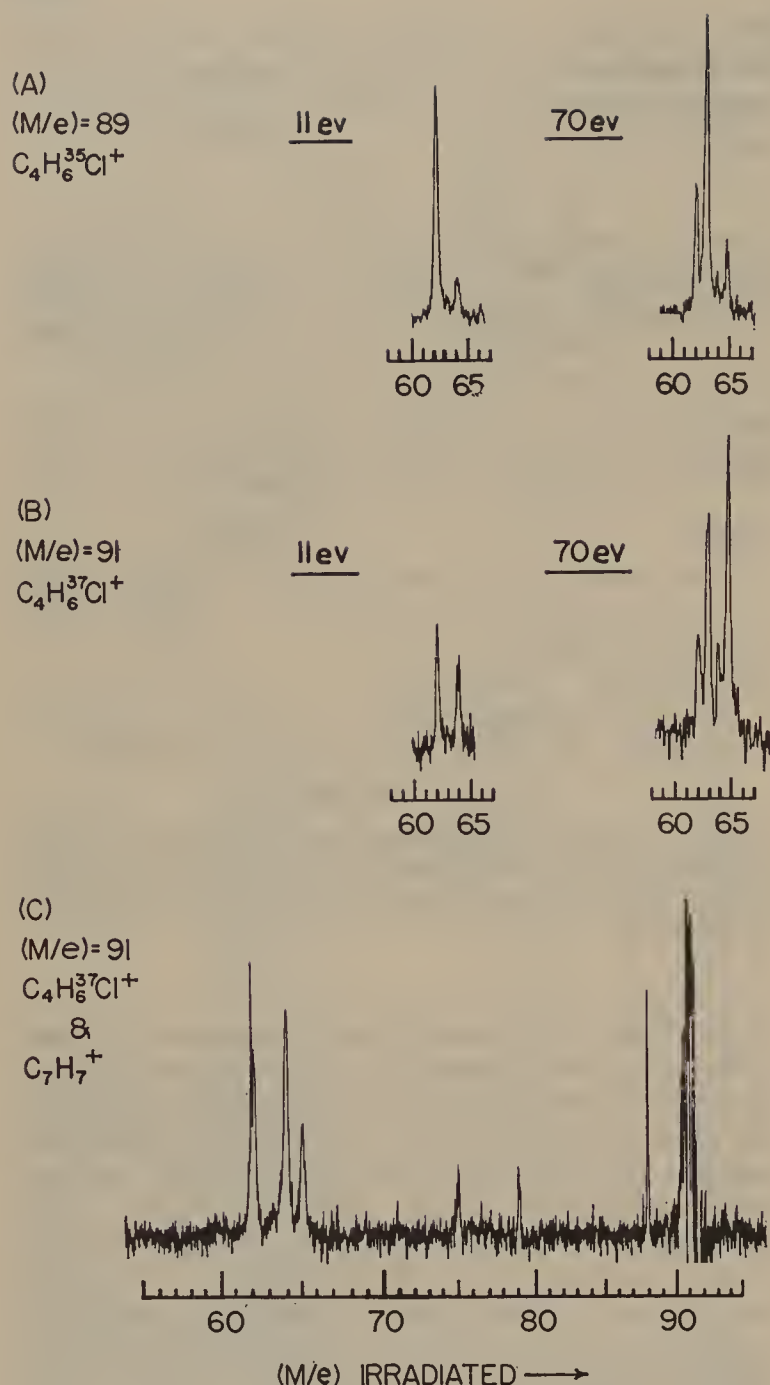
Figure 9. (A) and (B): Pulsed double-resonance spectra showing the relative contribution of the parent chlorine isotopes to the product chlorine isotopes for $C_4H_6Cl^+$ at 3×10^{-6} torr with 11 and 70 ev electron energy. (C): Pulsed double resonance spectra of m/e 91 products at 11 ev electron energy under conditions where high order reactions are observed.

where $CHCl_2^+$ is evident in Figure 7A with isotopic peaks at m/e 83, 85, and 87 visible. The peak in Figure 7A at m/e 73 probably corresponds to $C_3H_2Cl^+$. Its double-resonance spectrum consists of contributions from the parent ion and m/e 89. The m/e 89 reaction can be written

$$C_4H_6{}^{35}Cl^+ + C_2H_3Cl \longrightarrow C_3H_2{}^{35}Cl^+ + C_3H_7Cl \qquad (16)$$

and the contribution from the parent ion may proceed through reaction 12 which produces $C_4H_6{}^{35}Cl^+$.

$C_6H_7^+$ is produced in the sequence 8a–c. However, it remains as a large peak at 11 ev, and double resonance shows it to come mostly from m/e 88 and 90, with small contributions from m/e 89 and 91. The postulated reaction involving $C_4H_5Cl^+$ is

$$C_4H_5Cl^+ + C_2H_3Cl \longrightarrow C_6H_7^+ + HCl + Cl \qquad (17)$$

while the reaction of $C_4H_6Cl^+$ involves the loss of two HCl functions.

$$C_4H_6Cl^+ + C_2H_3Cl \longrightarrow C_6H_7^+ + 2HCl \qquad (18)$$

(A)
ION OBSERVED
(M/e)=103
$C_5H_6{}^{37}Cl^+$

73 75 77 79

(B)
(M/e)=101
$C_5H_6{}^{35}Cl^+$

73 75 77 79
(M/e) IRRADIATED ⟶
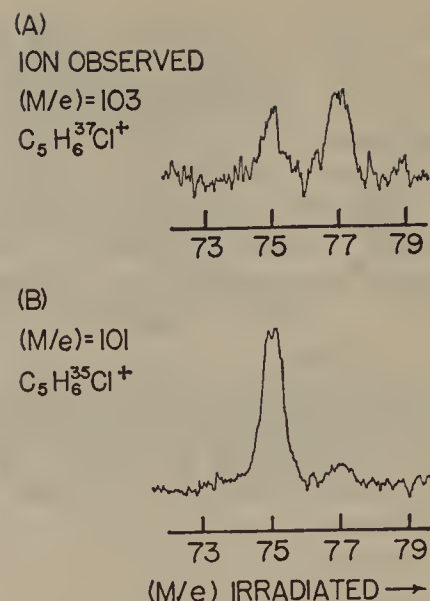
Figure 10. Pulsed double-resonance spectra showing the relative contributions of the $C_3H_4Cl^+$ ion chlorine isotopes to the chlorine isotopes in the $C_5H_6Cl^+$ product.

It becomes increasingly difficult to sort out the reactions in the higher mass range. Products involving m/e values up to 127 are given in Table II. The ions corresponding to these peaks can in most cases be produced by addition of product ions above to chloroethylene followed by elimination of HCl.

Table III. Observed Relative Contribution of Reactant Ion Isotopic Species to Product Ion

Reactant	Product	Relative contribution of reactant ion isotopic species to product ion[a]	
		^{35}Cl	^{37}Cl
$C_2H_3Cl^+$	$C_3H_4{}^{35}Cl^+$	0.88	0.12
	$C_3H_4{}^{37}Cl^+$	0.57	0.43
$C_2H_3Cl^+$	$C_4H_5{}^{35}Cl^+$	0.85	0.15
	$C_4H_5{}^{37}Cl^+$	0.55	0.45
$C_2H_3Cl^+$	$C_4H_6{}^{35}Cl^+$	0.87	0.13
	$C_4H_5{}^{37}Cl^+$	0.57	0.43
$C_2H_4Cl^+$	$C_4H_5{}^{35}Cl^+$	0.85	0.15
	$C_4H_6{}^{37}Cl^+$	0.42	0.58
$C_3H_4Cl^+$	$C_5H_6{}^{35}Cl^+$	0.88	0.12
	$C_5H_6{}^{37}Cl^+$	0.46	0.54

[a] Sum of ^{35}Cl and ^{37}Cl relative contributions set equal to unity.

An attempt was made to observe exchange reactions of $^{35}Cl^-$ with $^{37}Cl^-$ and $^{35}Cl^+$ with $^{37}Cl^+$ via reactions of the type

$$^{35}Cl^\pm + C_2H_3{}^{37}Cl \longrightarrow C_2H_3{}^{35}Cl + {}^{37}Cl^\pm \qquad (19)$$

but neither of these reactions could be detected using double resonance. The charge exchange reaction

$$C_2H_3{}^{35}Cl^+ + C_2H_3{}^{37}Cl \longrightarrow C_2H_3{}^{37}Cl^+ + C_2H_3{}^{35}Cl \qquad (20)$$

however was detected using double-resonance techniques.

No cyclotron resonance absorption signals were observed which could be attributed to the intermediate species expected in the above reactions, and no effects were observed in the pulsed double-resonance spectra of the products with strong irradiation at the m/e values of the corresponding intermediates.

The prominent ion–molecule reaction sequences observed in the cyclotron resonance spectra of chloroethylene are summarized in Figure 11.
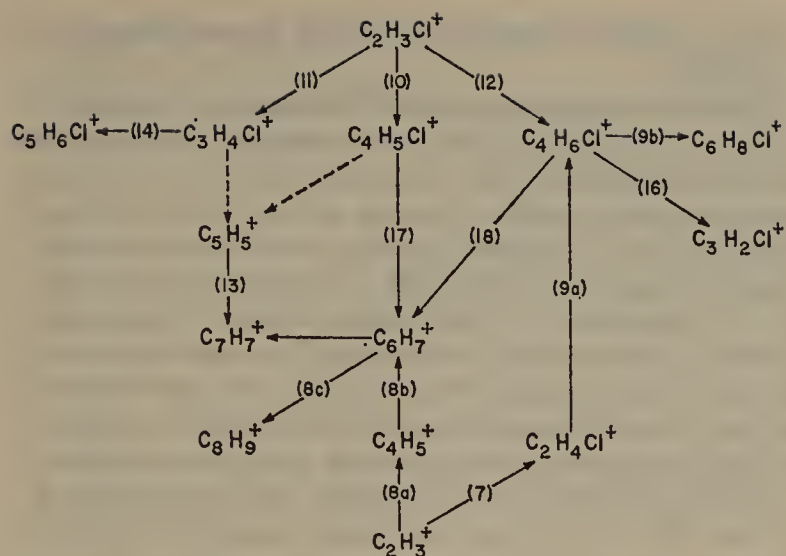
Figure 11   Reactions occurring in chloroethylene starting with $C_2H_3Cl^+$ and $C_2H_3^+$. The numbers refer to reactions in the text. The dashed lines indicate reactions which are inferred.

Figure 12.   Field-sweep single resonance spectrum of a 4:1 mixture of chloroethylene and methane at 70-ev electron energy and 2×10^{-5} torr.   Above m/e 62 peaks are distorted due to high ion densities.

Figure 13.   Field-sweep single-resonance spectrum of a 4:1 mixture of chloroethylene and perdeuteriomethane at 70-ev electron energy and 2×10^{-5} torr.

C.   Mixtures of Chloroethylene with Methane and Methane-d_4.

Figure 12 shows the spectrum of a mixture of methane and chloroethylene in the ratio 1:4. The products of two reactions known to occur in methane[15] are evident.

$$CH_4^+ + CH_4 \longrightarrow CH_5^+ + CH_3 \tag{21}$$

$$CH_3^+ + CH_4 \longrightarrow C_2H_5^+ + H_2 \tag{22}$$
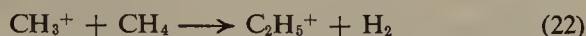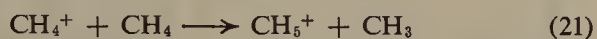
Reactions discussed above characteristic of chloroethylene are also apparent. The behavior of the spectrum above m/e 60, where the peaks are distorted, is related to high ion densities in the resonance cell which result from low-drift velocities at high magnetic field strengths. Certain peaks in Figure 12 are the result of reactions between methane ions and chloroethylene neutrals. The reactions verified by double resonance include

$$CH_3^+ + C_2H_3Cl \longrightarrow C_3H_5^+ + HCl \tag{23}$$

$$C_3H_5^+ + C_2H_3Cl \longrightarrow C_5H_7^+ + HCl \tag{24}$$

$$C_2H_5^+ + C_2H_3Cl \longrightarrow C_4H_7^+ + HCl \tag{25}$$

Only one reaction between chloroethylene ions and methane neutrals was identified.

$$C_2H_3^+ + CH_4 \longrightarrow C_3H_5^+ + H_2 \tag{26}$$
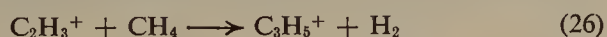
This reaction is known to occur as a tertiary process in methane.[15]

Figure 13 gives the complex single resonance spectrum obtained with a mixture of chloroethylene and methane-d_4 in the ratio 4:1. Proton- and deuteron-transfer reactions combined with reactions of the type observed in methane and chloroethylene account for many of the peaks. The purpose of examining the mixture was to see if DCl or HCl would be eliminated in the reaction

$$CD_3^+ + C_2H_3Cl \longrightarrow \begin{array}{l} C_3H_2D_3^+ \ (m/e \ 44) + HCl \\ C_3H_3D_2^+ \ (m/e \ 43) + DCl \end{array} \tag{27}$$
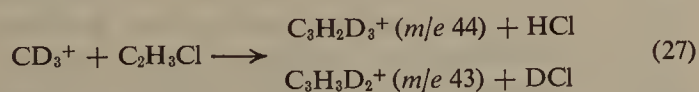
Irradiating the CD_3^+ caused a change in the absorptions observed at both m/e 43 and 44. Since the peaks at m/e 43 and 44 had other contributions (none of which involved CD_3^+ as a precursor) the relative yields of HCl and DCl in reaction 27 could not be accurately esti-

mated. These reactions confirm the generality of reaction 6. Since in the addition reaction of CD_3^+ both HCl and DCl are eliminated, it appears that proton transfers can occur very rapidly in the intermediate species. Rapid proton and deuteron transfers in intermediate species have been observed in the reaction of CD_4^+ with ethylene.[16]

IV.   Discussion

A.   Single-Resonance Spectra. There are several obvious advantages to observing directly ion–molecule reactions in their reactant mixtures at pressures below 10^{-4} torr. First, the reactions are with certainty bimolecular. Secondly, there is no need to extract ions for analysis thereby precluding interferences which may occur during the extraction process. Thirdly, the static electric fields in the cell do not produce a net acceleration of the ions with the result that reactions are observed either at thermal energies or at translational temperatures determined by the initial fragmentation following electron impact. Finally, the direct observation of the ion–molecule mixture is an essential requirement for the application of the double-resonance scheme for the identification of reactions. The resolution at 10^{-4} torr is >100 and can be simply improved by operation at higher magnetic field. At 3×10^{-5} torr the spectrum in Figure 3C shows no overlapping of adjacent mass peaks as high as m/e 127.

The cyclotron resonance line shape in the absence of terms which couple the equation of motion of various ionic species is Lorentzian[14]

$$A(\omega) = \frac{\dfrac{ne^2E_0^2v}{4m}}{v^2 + (\omega - \omega_c)^2} \tag{28}$$

(15) F. P. Abramson and J. H. Futrell, *J. Chem. Phys.*, **45**, 1925 (1966).

(16) F. W. Lampe and F. H. Field, *Tetrahedron*, **7**, 189 (1959).

where $A(\omega)$ is the power absorption, n is the number of ions, and ν is the collision frequency for momentum transfer. The absorption intensity varies inversely as the mass of the ionic species. If an icr spectrum is obtained by sweeping the magnetic field, the drift velocity of the ions in the cell changes according to eq 5 making n in eq 28 proportional to H and thereby to M. If ν is independent of the nature of the ionic species, then $A(\omega)$ should be an approximate measure of relative ion densities for a field-sweep spectrum. The general agreement of the low-pressure spectrum in Figure 3A with ref 13 substantiates these contentions. Difficulties are occasionally encountered when ion densities become sufficient for ion–ion interactions to distort the line shapes by disturbing the normal ion motions. The usual result is to give the line shape exhibited by the m/e 62 peak in Figure 12. The normal line shape can be obtained by lowering the electron emission current.

The variation of spectra with pressure as outlined in section IIIA is straightforward with the exception of the "high"-pressure spectrum at 4×10^{-4} torr shown in Figure 5 and the ^{35}Cl:^{37}Cl ratio in the parent ions. The species that remain at 4×10^{-4} torr appear to be remaining impurities and/or ions of unusual stability with regard to reaction with chloroethylene. At this pressure no parent or product ion evident at lower pressures could be observed.

With regard to the Cl isotope ratio it has been shown[14] in the case of a mixture of ^{20}Ne and ^{22}Ne isotopes that the single resonance spectrum will give an apparent value for the ratio of ^{20}Ne$^+$:^{22}Ne$^+$ which exceeds the ratio of the corresponding neutral species by as much as a factor of 4. The mechanism for this is related to the way in which the charge-transfer cross sections vary with the ion–molecule relative velocity. If a similar mechanism were operating in the case of the $C_2H_3^{35}Cl^+$ and $C_2H_3^{37}Cl^+$ ions, then the observed ratio $C_2H_3^{35}Cl^+$:$C_2H_3^{37}Cl^+$ could be greater than 3:1. As noted in section III, charge transfer between the two isotopes of the parent ion was observed. This may, however, not be important at 5×10^{-7} torr (Figure 3A). This leaves the observed ratio of $C_2H_3^{35}Cl^+$:$C_2H_3^{37}Cl^+$ to be attributed to an instrumental effect, possibly a consequence of the modulation-detection scheme. With drift modulation (see Figure 7) the ratio appears to be less than 3:1, although the resolution is poor. With field modulation no significant change of the ratio occurred with variation of modulation amplitude or frequency.

B. Significance of Observed Reactions in Chloroethylene. Reaction 6 appears to have considerable generality as a bimolecular electrophilic addition–elimination process governing reactions of ions with chloroethylene. The species which undergo this reaction with chloroethylene include both ions and ion radicals. At pressures above a few torr it might be expected that the intermediate species in reaction 6 could be stabilized by collisional deactivation. This is the case in the ion–molecule reactions occurring in the radiolysis of C_2H_4[17] where ionic addition produces species which are stabilized before fragmentation occurs. Evidence[17] for this is given by the appearance of a sequence of mass peaks corresponding to $(C_2H_4)_n^+$, indi-

(17) P. Kebarle, R. M. Haynes, and S. Searles, ref 4, Chapter 13.

cating successive addition without intermediate fragmentation.

The most significant result of this study is the identification of the origin of the chlorine atom retained in the product ion for the reactions in which the parent ion also contains a single chlorine atom. If the retained chlorine is that originally present in the parent neutral, then the isotopic distribution in these product ions will be the same as the isotopic distribution in the parent neutral, regardless of the identity of the chlorine isotope present in the reactant ion. Under these conditions if a particular chlorine isotope in the product is observed while the irradiating oscillator is swept, the irradiated ions will yield the product isotope in the ratio of 3:1. If the chlorine isotope in the ion product is retained from the parent ion then a particular chlorine isotope in the product exhibits a double-resonance peak only when irradiating the parent ion containing the same isotope. A third simple case obtains when the two chlorines in the intermediate species become equivalent and can be eliminated with equal probability. An analysis of the double-resonance effects to be expected in this case indicates that the ^{35}Cl and ^{37}Cl reactant ions will give contributions in the double-resonance spectrum of the ^{35}Cl and ^{37}Cl products in the ratios 7:1 and 3:5, respectively. Table IV shows the relative contributions of irradiated parent isotopes to each product ion isotope for the three cases considered.

Table IV. Calculated Relative Contribution of Reactant Ion Isotopic Species to Product Ion

Origin of Cl retained in product ion	Product Cl isotope	Relative contribution of reactant ion isotopic species to product ion[a]	
		^{35}Cl	^{37}Cl
Both chlorines retained with equal probability	^{35}Cl	0.875	0.125
	^{37}Cl	0.375	0.625
Chlorine retained from parent ion	^{35}Cl	1.0	0.0
	^{37}Cl	0.0	1.0
Chlorine retained from parent neutral	^{35}Cl	0.75	0.25
	^{37}Cl	0.75	0.25

[a] Sum of ^{35}Cl and ^{37}Cl relative contributions set equal to unity.

Reactions of the Parent Ion. As discussed in section III there are three competing reactions for the parent ion. These are

$$C_2H_3Cl^+ + C_2H_3Cl \longrightarrow \begin{cases} C_3H_4Cl^+ + CH_2Cl & (29a) \\ C_4H_5Cl^+ + HCl & (29b) \\ C_4H_6Cl^+ + Cl & (29c) \end{cases}$$
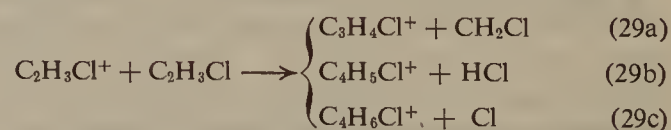
A comparison of the results given in Table III for reactions 29a–c with different possibilities considered in Table IV indicates that either of the two chlorine atoms present in the intermediate species can be eliminated with equal probability. Resonant charge exchange during the formation of a collision complex can provide a simple Cl atom equilibration mechanism for these three reactions. Two-step processes such as the charge-transfer reaction (20) followed by one of reactions 29a–c can also affect the observed relative contributions of reactant ion isotopic species to product ions. These effects can be recognized by their characteristic pressure and radiofrequency field dependence and probably

account for some of the discrepancies in the comparison of Tables III and IV.

Further mechanistic information on the reactions could obviously be obtained by using specifically deuterated chloroethylene. Although primary mass spectra of the various dichlorocyclobutanes are not yet available it would be of great interest to see what relationship they bear to the three primary reaction products obtained from the addition of $C_2H_3Cl^+$ to C_2H_3Cl. The results of the reaction of ethylene parent ions with ethylene have yielded results[2a] which strongly suggest that the intermediate decomposes to give products roughly analogous in abundance to those obtained in fragmentation of cyclobutane following electron impact. The reactions observed are

$$C_2H_4^+ + C_2H_4 \longrightarrow \begin{cases} C_3H_5^+ + CH_3 & (30a) \\ C_4H_6^+ + H_2 & (30b) \\ C_4H_7^+ + H & (30c) \end{cases}$$
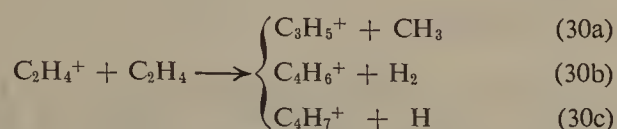
which are analogous to reactions 29a–c. Similar results have been obtained in the case of tetrafluoroethylene.[18] The evidence in all three cases suggests that the intermediate species formed in the reaction of parent ethylenic ions with the corresponding neutral molecule are strongly bonded entities.

Higher Order Reactions. In reaction 14 the observation of chlorine isotope transfers indicates (Table III) equivalence of the chlorine in the intermediate species. In this reaction the possibility of charge exchange in the collision complex leading to equilibration is eliminated, and the effect must be attributed to the formation of an intermediate species $(C_5H_7Cl_2^+)^*$ in which the chlorines are positioned at chemically equivalent sites. In reaction 9a equivalence of the chlorines in the intermediate species is again indicated (Table III), suggesting the possibility of rapid resonant proton transfer between the ionic and neutral reactants during the formation of the collision complex. Chlorine isotope effects

(18) G. A. W. Derwish, H. Galli, A. Giardini-Guidoni, and G. G. Volpi, *J. Am. Chem. Soc.*, **86**, 4563 (1964).

were not examined in the remaining higher order reactions because of the increasing complexity of competing reactions.

The formation of stable ionic species interrupts the general pattern of successive addition elimination reactions. The intensity of the $C_6H_7^+$ peak is quite large even at low pressures (Figures 3B and 4). This is probably the result of cyclization reactions producing protonated benzene (I). The fact that $C_7H_7^+$ is pro-

duced in a number of reactions is also indicative of its high stability, suggesting that the ion has the tropyllium structure (II).
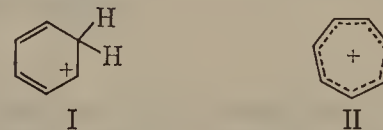
V. Conclusion

The above results quite clearly demonstrate the unique usefulness of ion cyclotron resonance for the study of ion–molecule reactions. The double-resonance technique used to follow the identity of chlorine isotopes is of course directly applicable to many reactions other than those studied here.[19] It is apparent that this technique can provide valuable information on the mechanisms of high-order ion–molecule reactions in complex systems and yield in addition qualitative evidence on the nature of reactive intermediates.

(19) J. L. Beauchamp and S. Sample, to be published.

Kinetics of the Reaction of Iodobenzene and Hydrogen Iodide. The Heat of Formation of the Phenyl Radical and Its Implications on the Reactivity of Benzene[1]

Alan S. Rodgers, David M. Golden, and Sidney W. Benson

Contribution from the Department of Thermochemistry and Chemical Kinetics, Stanford Research Institute, Menlo Park, California 94025. Received January 25, 1967

Abstract: The kinetics of the reaction of iodobenzene and hydrogen iodide were studied in the gas phase from 375 to 500°. The rate data were consistent with the free-radical mechanism

$$I_2 + M \overset{}{\rightleftarrows} 2I + M, \quad C_6H_5I + I \overset{1}{\underset{2}{\rightleftarrows}} C_6H_5\cdot + I_2, \quad \text{and} \quad C_6H_5\cdot + HI \overset{3}{\underset{4}{\rightleftarrows}} C_6H_5H + I$$
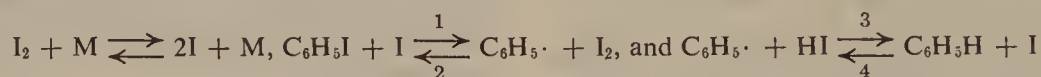
and resulted in $\log(k_1, \text{l. mole}^{-1}\text{ sec}^{-1}) = (11.36 \pm 0.06) - (28.4 \pm 0.2)/\theta$. The assumption that $E_2 = 0 \pm 1$ kcal/mole yields $\Delta H_f°_{298}(C_6H_5\cdot, g) = +80.0 \pm 1$ and $DH°_{298}(C_6H_5-H) = 112.3 \pm 1$ kcal/mole. This is 5 to 10 kcal/mole higher than previous literature values, but nevertheless is found to be consistent with kinetic data on the pyrolysis of iodo- and bromobenzene. The discrepancy between this present work and data from radical "abstraction" reactions from benzene cannot be reconciled, indicating that these reactions proceed by a complex mechanism. A mechanism for "abstraction" from benzene is proposed and illustrated for the thermal chlorination and bromination of substituted benzenes. It is shown to be in quantitative, as well as qualitative, agreement with the available data.

The reactions of organic iodides with hydrogen iodide proceed by the free-radical mechanism[2]

$$I_2 + M \overset{}{\rightleftarrows} 2I + M \qquad K_{I_2}$$

$$RI + I \overset{1}{\underset{2}{\rightleftarrows}} R\cdot + I_2 \qquad (1, 2)$$

$$R\cdot + HI \overset{3}{\underset{4}{\rightleftarrows}} RH + I \qquad (3, 4)$$
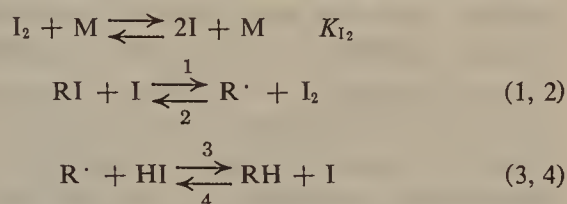
This mechanism has been independently verified for $RH = CH_4$ by kinetic measurements on $CH_3I + HI$[3] and $CH_4 + I_2$,[4] and equilibrium measurements for $CH_3I + HI \rightleftarrows CH_4 + I_2$.[5] A study of the kinetics of the conversion of RI results in Arrhenius parameters for k_1 (i.e., A_1 and E_1). These combined with the assumption that $E_2 \cong 0$[6] yields a value for $\Delta H_{1,2}°$ and, therefore, $\Delta H_f°(R\cdot)$ provided $\Delta H_f°(RI)$ is known. The values of $\Delta H_f°(R\cdot)$, so obtained, define by eq 5 the bond dissociation energies in organic molecules.

$$DH°(R-X) = \Delta H_f°(X) + \Delta H_f°(R\cdot) - \Delta H_f°(R-X) \quad (5)$$

In this paper we consider the kinetics of the reaction of iodobenzene with hydrogen iodide and the heat of formation of the phenyl radical.

Experimental Section

The reaction of phenyl iodide with HI was followed by measuring the iodine partial pressure spectrophotometrically (λ 500 mμ) as a function of time. The temperature range covered was 375 to 500°. The apparatus has been described in detail previously.[6]

a. Materials. Iodobenzene was obtained from Eastman Organic Chemical Co. and purified by gas–liquid chromatography on an F and M Prepmaster, using an SE-30 silicone oil column. Glc analysis showed it to be >99% pure. The benzene was Baker Reagent Grade and was used without further purification. Iodine was obtained from the Mallinckrodt Chemical Co. and was vacuum sublimed prior to use. Anhydrous HI was obtained from the Matheson Co. and purified by vacuum distillation.

b. Procedure. At each experimental temperature, the absorbance coefficient, α^λ, of C_6H_5I, HI, I_2, and C_6H_6 (equivalent to the absorption coefficient times the path length) was determined at 270, 280, and 500 mμ. Beer's law was found to hold to an OD of 2.0 to within $\pm$2%; 380 mμ was used as an optical window ($\alpha^{380}_{C_6H_5I} \sim 5 \times 10^{-4}$ torr^{-1}). [At the higher temperatures, 460 to 500°, it was observed that phenyl iodide decomposed slightly as indicated by an increase in absorbance at 270, 280, and 500 mμ. This was, however, severely inhibited by I_2, so that all experiments (including calibration of C_6H_5I at 500°) at these temperatures were performed with from 1 to 5 torr of I_2 added initially.]

The absorbance of the evacuated cell ($\sim 10^{-5}$ torr) was determined at 270, 280, 380, and 500 mμ. Then the desired pressure of I_2 (when used) was admitted and its absorbance measured at these wavelengths, whereupon C_6H_5I was admitted and the absorbance and pressure again recorded. The agreement between the measured pressure and that calculated from the absorbance at 270 and 280 mμ was better than 2%. The desired pressure of HI was then expanded into the vessel and the absorbance at 500 mμ was recorded as a function of time with a synchronous motor chart drive. Kinetic measurements were made exclusively at 500 mμ, as this was the most sensitive wavelength for following the reaction (0.005 torr of I_2 could be detected) and gave a direct determination of the I_2 partial pressure (no other species absorbs at 500 mμ). The rate of the reaction was determined by the approximation d(I_2)/dt = $\Delta(I_2)/\Delta t$. The interval $\Delta(I_2)$ was adjusted to yield an estimated error in d(I_2)/dt of 2 to 5%.

Results

Preliminary experiments were made at 400 and 460° to verify the stoichiometry of the reaction. These results are summarized in Table I and indicated that no important side reactions occurred.

A steady-state treatment of the mechanism, neglecting reaction 4, results in the rate expression

$$\frac{d(I_2)}{dt} = \frac{K_{I_2}^{1/2}k_1(C_6H_5I)(I_2)^{1/2}}{1 + \left(\dfrac{k_2}{k_3}\right)\dfrac{(I_2)}{(HI)}} \quad (6)$$

(1) (a) This investigation was supported in part by a research grant (AP 00353-03) from the Air Pollution Division, Public Health Service, U. S. Department of Health, Education, and Welfare. (b) Presented in part at the 2nd Western Regional Meeting of the American Chemical Society, San Francisco, Calif., Oct 1966 and at the 153rd National Meeting of the American Chemical Society, Miami, Fla., April 1967.

(2) S. W. Benson and H. E. O'Neal, *J. Chem. Phys.*, **34**, 514 (1961).

(3) M. C. Flowers and S. W. Benson, *ibid.*, **38**, 882 (1963).

(4) C. A. Goy and H. O. Pritchard, *J. Phys. Chem.*, **69**, 3040 (1965).

(5) D. M. Golden, R. Walsh, and S. W. Benson, *J. Am. Chem. Soc.*, **87**, 4053 (1965).

(6) M. Christie, *Proc. Roy. Soc.* (London), **A224**, 411 (1958), has measured for $CH_3 + I_2 \longrightarrow CH_3I + I$ a value of $E_2 < 1$ kcal/mole, and this has been supported by ref 4 and 5.

Table I. Comparison of the Observed Increase in Iodine and Decrease in Iodobenzene Partial Pressures for the Reaction $C_6H_5I + HI \rightarrow C_6H_6 + I_2$

Temp, °C	$(I_2) - (I_2)_0$, torr; λ 500 mμ	$(C_6H_5I)_0 - (C_6H_5I)$, torr λ 280 mμ	λ 270 mμ
397.5[a]	1.47	1.58	1.49
	2.88	2.96	2.89
	3.93	3.98	3.91
	4.70	4.69	4.59
463.5[b]	2.76	2.77	2.74
	4.22	4.35	4.24
	5.09	5.24	5.16
	5.65	5.81	5.75

[a] $(C_6H_5I)_0 = 9.08$, $(HI)_0 = 11.1$, $(I_2)_0 = 0.07$ torr. [b] $(C_6H_5I)_0 = 7.1$, $(HI)_0 = 18.1$, $(I_2)_0 = 4.4$ torr.

This equation may be rearranged to yield

$$\frac{(I_2)}{(HI)} = \frac{K_{I_2}^{1/2}k_1k_3}{k_2}\frac{(C_6H_5I)(I_2)^{1/2}}{d(I_2)/dt} - \frac{k_3}{k_2} \quad (7)$$

When the ratio I_2/HI fell in the range 0.1 to 2.0, as in the experiments at 435 to 500°, the data were treated according to eq 7, and the values of k_3/k_2 and k_1[7] were obtained directly. A plot of the data at 500° is given in Figure 1. The value of k_3/k_2 obtained in this manner was estimated to be accurate to 8% and k_1 to 5%, due to the compensating changes in slope and intercept.

For the experiments at 375 to 400°, ratios of I_2/HI were in the range 0.01 to 0.1 so that the denominator of the right-hand side of eq 6 was ~1. Under such conditions the data were appropriately treated according to eq 6 with a value of k_2/k_3 extrapolated from the data in the range 435 to 500°. The value so obtained was 5 ± 0.5 and was used at 400 and 375°. Note that a 10% error in k_2/k_3 will yield less than a 2% error in k_1. All the data obtained at 404° are given in Figure 2. The three runs included span a threefold variation in HI concentration and provide direct evidence that the rate is independent of the HI concentration and dependent on the square root of the I_2 concentration at low I_2/HI ratios, as predicted by the mechanism. The slope of this curve gave $K_{I_2}^{1/2}k_1$ from which k_1 may be derived;[7] the estimated uncertainty was 5%. This value of k_1 may then be used in an inhibited run (i.e., high value of $(I_2)/(HI)$, see Table II) to experimentally determine $k_3/k_2 = 0.215$ at 402°. [The data represented by open circles in Figure 2 show that the initial rate of formation of iodine is greater than that predicted. This was generally observed in all runs at less than 1% conversion, as well as in the pyrolysis of 100 torr of HI at 400°. We suspect that this enhanced rate of formation of iodine resulted from the oxidation of HI by trace amounts (10^{-3} to 10^{-2} torr) of oxygen. The stoichiometry may be $4HI + O_2 \rightarrow 2I_2 + 2H_2O$.]

The experimental values for k_1 and k_3/k_2 are summarized in Table II and yield

$$\log (k_1, \text{l./mole sec}) = 11.36 \pm 0.06 - \frac{28.4 \pm 0.2}{\theta} \quad (8)$$

$$\log (k_3/k_2) = -0.14 \pm 0.3 - \frac{1.6 \pm 1}{\theta} \quad (9)$$

The errors are one standard deviation; $\theta = 2.303RT$ kcal/mole.

(7) Thermodynamic data for $K_{I_2}^{1/2}$ were obtained in "JANAF Interim Thermochemical Tables," D. P. Stull, Ed., Dow Chemical Co., Midland, Mich., 1963.
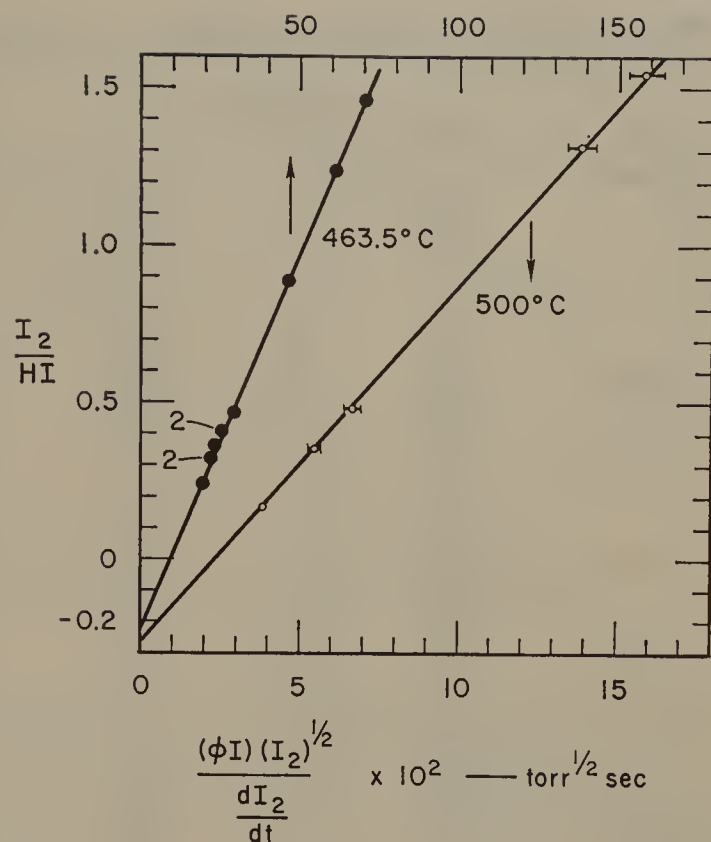
Figure 1. Plot of $(I_2)/(HI)$ vs. $(C_6H_5I)(I_2)^{1/2}/$rate at 460 and 500° Numerals denote overlapping data.
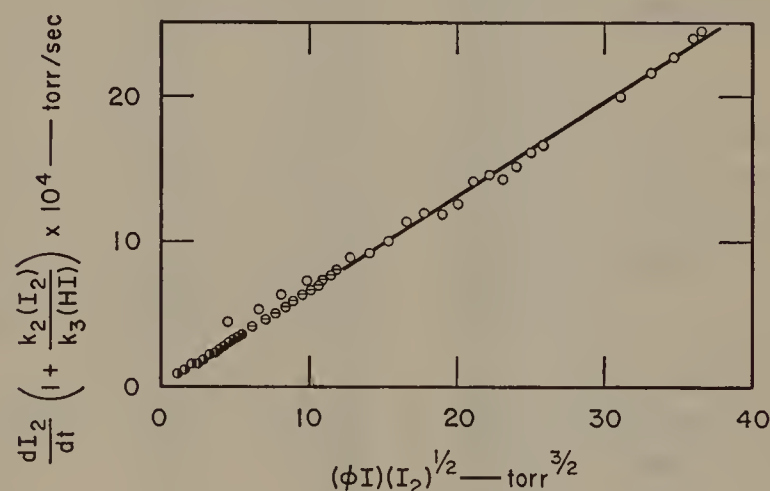
Figure 2. Plot of rate$(1 + k_2(I_2)/k_3(HI))$ vs. $(C_6H_5I)(I_2)^{1/2}$ at 404°. Initial conditions in torr and per cent reaction of last point are: O, $C_6H_5I = 21.1$, $HI = 59.4$, 44%; ⊖, $C_6H_5I = 11.7$, $HI = 24.5$, 11%; ⊙, $C_6H_5I = 5.75$, $HI = 44.7$, 30%.

These experimental data may be combined with the thermodynamic data of Table III and the assumption that $E_2 = 0 \pm 1$ kcal/mole to yield the following rate constants at the mean temperature 700°K (units of l./mole sec): $k_2 = 10^{9.74}$, $k_3 = 10^{9.60 - 1.6/\theta}$, and $k_4 = 10^{12.18 - 43.0/\theta}$. The logarithm of Arrhenius preexponential factor (log A) in k_1 is 11.36 (l. mole^{-1} sec^{-1} units) and falls in the range of values previously reported, namely 11.4 for CH_3I,[3] 11.0 for C_2H_5I,[8a] and 10.9 for CH_3COI.[8b] The A factor may be expressed in terms of collision theory as

$$A = pZe^{1/2}$$

where p is a steric factor, generally less than unity, and Z is the collision frequency. The $e^{1/2}$ arises as a result

(8) (a) D. B. Harley and S. W. Benson, J. Chem. Phys., 39, 132 (1963); (b) H. E. O'Neal and S. W. Benson, ibid., 37, 540 (1962); (c) R. Walsh and S. W. Benson, J. Am. Chem. Soc., 88, 4570 (1966).

Table II. Kinetic Data for the Reaction $C_6H_5I + HI \rightleftharpoons C_6H_6 + I_2$

| Temp, °C | Pressure, torr | | | $d(I_2)/dt \times 10^3$ torr sec^{-1} | $k_1 \times 10^3$, torr^{-1} sec^{-1} | k_3/k_2 | Expt no. | $K_{I_2}^{1/2}$, torr$^{1/2}$ |
	C_6H_5I	HI	I_2					
500	7.58	42.28	7.73	54.6				
	4.60	44.30	10.71	31.6				
	4.67	14.87	5.26	19.6				
					44.0	0.26	3	9.82×10^{-2}
	3.38	13.59	6.54	13.1				
	8.03	4.03	5.27	13.2				
	7.66	3.66	5.64	11.4				
463.5	6.38	7.08	6.29	3.45				
	5.26	5.96	7.41	2.34				
	4.73	5.43	7.94	1.89				
	6.13	17.13	5.37	6.32				
					19.9	0.22	3	5.435×10^{-2}
	4.34	15.34	7.16	4.01				
	16.14	13.84	3.32	15.0				
	15.28	12.98	4.18	13.6				
	14.51	12.21	4.95	12.5				
436.5	2.24	8.94	2.86	0.490				
	3.18	9.88	1.92	0.729				
	7.42	10.32	1.98	1.76				
					8.82	0.25	3	3.374×10^{-2}
	4.83	7.73	4.57	0.925				
	20.0	4.84	1.75	3.32				
	18.91	3.71	2.89	2.40				
435.5	10.32	9.62	5.95	2.00				
	9.59	8.89	6.69	1.74				
					9.15	0.22	1	3.313×10^{-2}
	7.58	6.88	8.70	1.02				
	6.95	6.25	9.33	0.831				
404[a]	20.63	58.93	0.47	0.887				
	19.85	58.15	1.25	1.32				
	19.31	57.61	1.79	1.45				
	11.32	24.12	0.38	0.423				
	11.14	23.94	0.56	0.484	3.62	0.20[b]	3	1.81×10^{-2}
	10.83	23.63	0.87	0.533				
	5.54	44.54	0.21	0.181				
	5.20	44.20	0.55	0.245				
402[a]	4.43	43.43	1.32	0.292				
	7.95	20.05	0.25	0.215				
	7.80	19.90	0.40	0.260				
	7.54	19.64	0.66	0.289				
					3.42	0.20[b]	2	1.735×10^{-2}
	3.98	11.38	0.25	0.105				
	3.75	11.15	0.50	0.125				
402[c]	3.36	10.76	0.89	0.132				
	20.73	3.43	8.77	0.282	3.42	0.22		
375[a]	20.25	2.95	9.25	0.232	3.42	0.21		
	5.74	9.04	0.061	0.0187				
	5.71	9.01	0.093	0.0234				
	5.67	8.97	0.131	0.0280				
					1.48	0.20[b]	2	0.971×10^{-2}
	9.63	11.43	0.0715	0.0364				
	9.57	11.37	0.136	0.0467				
	9.49	11.29	0.213	0.0575				

[a] Representative data. [b] Extrapolated value. [c] Experimental determination of k_3/k_2.

of the $T^{1/2}$ dependence in Z. By taking the mean collision diameter as 5 A at 725°K, log $Ze^{1/2} = 11.52$, so that $p \cong 1$. A value of p near unity implies little need for orientation in the collision pair and corresponds to a loose transition state in the language of transition-state theory.[9]

The value obtained for log $(A_3/A_2) = -0.14 \pm 0.3$ compares favorably with previous determinations which have yielded[8a-c] -0.5 ± 0.3. From this comparison, one might prefer the lower end of the error range, i.e., log $A_3/A_2 = -0.5$, and consideration of log A_4 reenforces this preference. For reaction 4, at 725°K

(9) S. W. Benson, "Foundation of Chemical Kinetics," McGraw-Hill Book Co., Inc., New York, N. Y., 1960, pp 271–781.

and a mean collision diameter of 5 A, log $Ze^{1/2} = 11.75$ (l. mole^{-1} sec^{-1} units). This is about 0.4 log unit lower than given above and would require $p \cong 3$ or, on the other hand, a mean diameter of about 8 A. Neither of these alternatives is readily justified, and therefore, they indicate a more negative value for log A_3/A_2. Consequently, the preferred values for k_3 and k_4, based upon log $(k_3/k_2) = -0.5 - (0.4/\theta)$, become (l. mole^{-1} sec^{-1} units) log $k_3 = 9.24 - (0.4/\theta)$ and log $k_4 = 11.82 - (41.8/\theta)$. From the assumption that $E_2 = 0$, we have $\Delta H_{1,2}°(700°K) = 28.4 \pm 1$ kcal/mole, this value corrected to 298° yields $\Delta H_{1,2}°(298°K) = 28.9 \pm 1$ kcal/mole, and therefore, $\Delta H_f°_{298}(C_6H_5\cdot,g) = +80.0 \pm 1$ kcal/mole. This may be used

Table III. Summary of Thermodynamic Data for Ideal Gas at 1 Atm[a]

Compd	$S°_{298}$, eu	$\Delta H_{f}°_{298}$, kcal/mole	C_p, cal deg^{-1} mol^{-2} 298°	500°	700°	$S°_{700}$, eu	$\Delta H_{f}°_{700}$, kcal/ mole
I_2	62.3	14.9	8.8	8.9	9.0	69.9	0.0
I	43.2	25.5	5.0	5.0	5.0	47.4	18.3
HI	49.4	6.3	7.0	7.1	7.4	55.4	−1.5
C_6H_6[b]	64.3	19.8	19.5	32.8	41.8	90.3	16.0
$C_6H_5\cdot$[c]	69.2	...	19.2	31.5	39.5	94.1	...
C_6H_5I[d]	84.8	40.5 ± 0.2	24.3	36.9	44.7	109.2	30.5

[a] Data from ref 7, unless indicated. [b] "Selected Values of Physical and Thermodynamic Properties of Hydrocarbons and Related Compounds," American Petroleum Institute, Carnegie Press, Pittsburgh, Pa, 1953. [c] Estimated from benzene, assuming 3000-, 1400-, and 1200-cm^{-1} vibrational frequencies have been lost. [d] $S°$ and C_p from D. H. Whiffen, *J. Chem. Soc.*, 1350 (1956); $\Delta H_f°(l)$ from A. S. Carson, E. M. Carson, and B. Wilmshurst, *Nature*, **170**, 320 (1952); and L. Smith, *Acta Chem. Scand.*, **10**, 884 (1956); ΔH_v from D. R. Stull, *Ind Eng. Chem.*, **39**, 517 (1947).

Figure 3. Arrhenius plot for the reaction $C_6H_5I + I \rightarrow C_6H_5\cdot + I_2$. Numerals indicate number of combined experiments.

with eq 5 to yield $DH°_{298}(C_6H_5-I) = 65.0 \pm 1$ kcal/mole and $DH°_{298}(C_6H_5-H) = 112.3 \pm 1$ kcal/mole.

Discussion

Several values for $DH°_{298}(C_6H_5-H)$, ranging from 102 to 107 kcal/mole, have been previously reported and these will be considered separately.

Butler and Polanyi[10] have studied the pyrolysis of C_6H_5I at 510° in a flow system with H_2 carrier gas. The partial pressure of C_6H_5I was 30 μ, and the reaction was carried to ~3% completion (Figure 3). Under these conditions, the primary mode of decomposition is[11]

$$C_6H_5I \longrightarrow C_6H_5\cdot + I \quad (10)$$
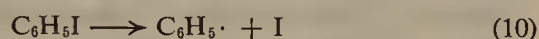
The Arrhenius parameters for k_{10} are given by transition state theory as

$$k_{10} = \frac{ekT}{h}\exp\left(\frac{\Delta S^{\ddagger}}{R} - \frac{E_a}{\theta}\right) = 10^{14.3 - (E/\theta)} \text{ sec}^{-1} \quad (11)$$

in which a value of $\Delta S^{\ddagger} = 3 \pm 2$ eu has been assumed.[12] The measured value for k_{10} at 783°K is $10^{-2.1}$ sec^{-1} and yields $E_{10} = 59$ kcal/mole; assuming $E_{-10} \cong 0$, then $\Delta H_{10}°(800°K) = \Delta E_{10}°(800°K) + RT_{mean} = 60.6$ kcal/mole. Correcting to 298°K yields $DH°_{298}(C_6H_5-H) = 108$ kcal/mole.

Ladacki and Szwarc[13] have measured the rate of pyrolysis of bromobenzene from 1050 to 1150°K, using the toluene carrier technique. They found that the rate-limiting step was

$$C_6H_5Br \longrightarrow C_6H_5\cdot + Br \quad (12)$$
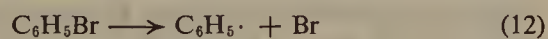
and a least-squares analysis of their results gave

$$\log k_{12} = 13.3 - (70.9/\theta) \text{ sec}^{-1}$$

With the assumption that $E_{-12} = 0$, then

$$\Delta H_{12}°(1100°K) = 70.9 + RT_{mean} = 73 \text{ kcal/mole}$$

$\langle \Delta C_p \rangle$ from 1100 to 300°K is essentially zero, so that

$\Delta H_{12}°(298°) = 73$ kcal/mole, and from the heat of formation[14,15] of bromobenzene, $DH°_{298}(C_6H_5-H) = 105.5$ kcal/mole. However, as in the case of iodobenzene, the entropy of activation should be positive rather than negative, a value of $\Delta S^{\ddagger} = 3 \pm 2$ eu being preferred. This results in $\log k_{12} = 14.3 - (75.9/\theta)$ from the observed rate constant of 0.13 sec^{-1} at 1080°K, and yields $DH°_{298}(C_6H_5-H) = 110.5$ kcal/mole. It should also be noted that these parameters yield an Arrhenius curve barely distinguishable from that given by Ladacki and Szwarc.

Within the different experimental scatter then, the pyrolysis data are found to yield bond dissociation energies consistent with the present work. Duncan and Trotman-Dickenson[16] have studied the kinetics of reaction 13 and combined their results with those of Trotman-Dickenson and Steacie[17] on reaction −13 to obtain $DH°_{298}(C_6H_5-H) = 102$ kcal/mole.

Fielding and Pritchard[18] have obtained Arrhenius parameters for reactions 13 and 14. Combining these values with those for the reverse reactions,[17,19,20a] they obtained $DH°(C_6H_5-H) = 105$ and 107 kcal/mole.

$$C_6H_5\cdot + CH_4 \rightleftarrows C_6H_6 + CH_3 \quad (13)$$

$$C_6H_5\cdot + CF_3H \rightleftarrows C_6H_6 + CF_3 \quad (14)$$

These values are based upon the assumption that the reverse reactions (−13 and −14) take place as direct abstraction reactions.[16] However, Whittle and coworkers[20] have presented convincing evidence that "abstraction" of hydrogen from the aromatic ring by trifluoromethyl radicals occurs *via* addition to form a cyclohexadienyl radical and subsequent disproportionation. Szwarc and Levy[21] have shown that methyl radicals add to benzene at a rate competitive with the abstraction of hydrogen from isooctane, as do trifluoro-

(10) E. T. Butler and M. Polanyi, *Trans. Faraday Soc.*, **39**, 19 (1943).

(11) The I partial pressure is too low for reaction 1 to compete, *i.e.*, $k_1(I)/k_{10} \lesssim 0.1$.

(12) For this bond-breaking reaction, one would expect a slightly positive entropy of activation. The value assumed corresponds to $A_{-10} = 10^{9.5}$ l./mole sec and appears reasonable in view of the fact that A_2 is $10^{9.7}$ l./mole sec.

(13) M. Ladacki and M. Szwarc, *Proc. Roy. Soc.* (London), **A219**, 341 (1953).

(14) A. S. Carson, E. M. Carson, and B. Wilmshurst, *Nature*, **170**, 320 (1952).

(15) D. R. Stull, *Ind. Eng. Chem.*, **39**, 517 (1947).

(16) F. J. Duncan and A. F. Trotman-Dickenson, *J. Chem. Soc.*, 4672 (1962).

(17) A. F. Trotman-Dickenson and E. W. R. Steacie, *J. Chem. Phys.*, **19**, 329 (1951).

(18) W. Fielding and H. O. Pritchard, *J. Phys. Chem.*, **66**, 821 (1962).

(19) G. O. Pritchard, H. O. Pritchard, H. I. Schiff, and A. F. Trotman-Dickenson, *Trans. Faraday Soc.*, **52**, 849 (1956).

(20) (a) S. W. Charles and E. Whittle, *ibid.*, **56**, 794 (1960); (b) S. W. Charles, J. T. Pearson, and E. Whittle, *ibid.*, **57**, 1356 (1961); (c) R. D. Giles and E. Whittle, *ibid.*, **62**, 128 (1966).

(21) M. Levy and M. Szwarc, *J. Am. Chem. Soc.*, **77**, 1949 (1955).

methyl radicals.[22] It therefore appears quite reasonable to expect the gas-phase reactions of methyl and trifluoromethyl radicals with benzene to be similar, so that the reported kinetic parameters[17,19] are not applicable to reactions −13 and −14. Indeed, the discrepancy between the values reported by Trotman-Dickenson[16] and Pritchard[18] for $DH^\circ_{298}(C_6H_5-H)$ and the present work may be taken as evidence for a more complex mechanism for "abstraction" in benzene.[23] The high value for $DH^\circ_{298}(C_6H_5-H)$ tends to make this a general conclusion which may be illustrated by a detailed consideration of the thermal chlorination and bromination of substituted benzenes.

These reactions, which result in nuclear substitution, have been studied by Kooyman and co-workers.[24] They have treated their data qualitatively and suggested a one-step bimolecular mechanism. We, however, feel that a free-radical mechanism, involving cyclohexadienyl radicals and cyclohexadiene as intermediates, is not only in qualitative accord with the experimental data, but is also in quantitative agreement with the kinetic observations for chlorination and semiquantitative agreement for bromination.[25]

The proposed mechanism, illustrated for *para* addition and *meta* substitution, is
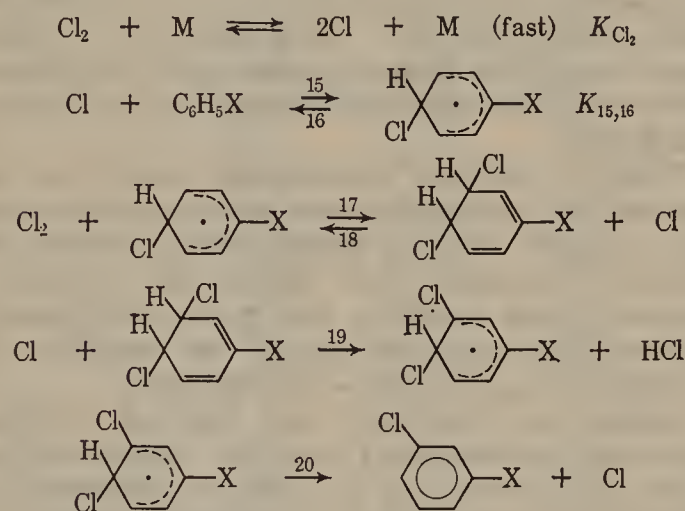
This yields, with the usual steady-state assumption

$$\frac{d(\text{product})}{dt} = \frac{k_{17}k_{19}}{k_{18} + k_{19}} K_{15,16} K_{Cl_2}^{1/2} (C_6H_5X)(Cl_2)^{3/2} \tag{21}$$

Applying this equation to the data (Table IV) on chlorination,[24] we find for X = CF₃

$$\frac{k_{17}k_{19}}{k_{18} + k_{19}} K_{15,16} = 10^{6.5 + 9/\theta} \tag{22}$$

From the Arrhenius parameters assignable to k_{17}, k_{18}, and k_{19} (see Appendix), we obtain

$$\frac{k_{17}k_{19}}{k_{18} + k_{19}} \cong 10^{10 - 3/\theta} \text{ l. mole}^{-1} \text{ sec}^{-1} \tag{23}$$

(22) A. P. Stefani, L. Herk, and M. Szwarc, *J. Am. Chem. Soc.*, **83**, 4732 (1961); A. P. Stefani and M. Szwarc, *ibid.*, **84**, 3661 (1962).
(23) The average of ref 16 and 18 gives $E_{13} = 9.3 \pm 2$ kcal/mole. This combined with $\Delta H_{13}° = -8.3 \pm 1.4$ kcal/mole from the present work results in $E_{-13} = 17.6 \pm 2.5$ kcal/mole for direct abstraction.
(24) E. C. Kooyman, "Advances in Free Radical Chemistry," Vol. **1**, Academic Press Inc., New York, N. Y., 1965, p 137.
(25) (a) R. J. Albers and E. C. Kooyman, *Rec. Trav. Chem.*, **83**, 930 (1964); (b) J. de Graaf and H. Kwart, *J. Phys. Chem.*, **67**, 1458 (1963).

and from eq 23

$$K_{15,16}(700°K) = 10^{-3.5 + 12/\theta} \text{ l. mole}^{-1} \text{ sec}^{-1} \tag{24}$$

Under typical reaction conditions, this gives a negligible steady-state concentration of diene of about 0.3 mole % C₆H₅CF₃. At lower temperatures cyclohexadiene and other addition products will represent an appreciable part of the over-all yield, as is observed in the photochlorination of benzene and its derivatives.[26]

The uncertainties in (24) should be less than a power of ten in the preexponential factor and 3 kcal/mole in the activation energy so that similar limits hold for (24). Therefore

$$\Delta H_{15,16}° = \Delta E_{15,16}° - RT_{mean} = -13.4 \pm 3 \text{ kcal/mole} \tag{25}$$

This leads to a value (see Appendix) of 25.5 ± 3 kcal/mole for the stabilization energy of the substituted cyclohexadienyl radical, which is in good agreement with the value of 24.5 ± 3 kcal/mole derived from the data of Suart[27] and Benson and Shaw[28] for cyclohexadienyl radical. The data for bromination (Table IV)

Table IV. Rate Data for the Chlorination and Bromination of Benzotrifluoride in the Gas Phase

Temp, °C	Cl₂, mmoles/l.[a]	% conversion[b]	Contact time, sec	Log $(k_{17}k_{19}K_{15,16}/k_{18} + k_{19})$[c]	% conversion (calcd)
350	2.4	40	177	9.65	40[d]
400	1.2	39	146	9.42	39
450	1.08	50	140	9.07₃	58
	Br₂				
400	4.8	28	142	6.50	28[e]
450	4.17	37	107	6.41	42

[a] Steady state. [b] Based on C₆H₅CF₃. [c] Log $K_{Cl_2}^{1/2} = 1.86 - 28.6/\theta$; log $K_{Br_2}^{1/2} = 1.75 - 22.6/\theta$ from ref 7; $\theta = 2.303RT$ kcal/mole. [d] Calculated by eq 22 and 23. [e] Calculated by eq 22 and 30.

lead to the following relationship for the relevant rate constants

$$\log\left(\frac{k_{17}k_{19}}{k_{18} + k_{19}} K_{15,16}\right) = (6.5 \pm 1) - (0 \pm 3)/\theta \tag{26}$$

and are also consistent with the observed value of the cyclohexadienyl stabilization energy.

The rapid exchange reactions observed by Kooyman and co-workers[24] can readily be accounted for by reactions 15 and 16 and would be expected to be fast when $DH°(C-X) < DH°(C-Y)$.

Thus, the reaction of chlorine with nitrobenzene (Y = Cl and X = NO₂) has been reported to occur quantitatively at 275°. The rate of exchange will be given by

$$\text{rate} = k_{15'}K_{Cl_2}^{1/2}(C_6H_5NO_2)(Cl_2)^{1/2}$$

(26) H. P. Smith, W. A. Noyes, Jr., and E. J. Hart, *J. Am. Chem. Soc.*, **55**, 4444 (1933); E. J. Hart and W. A. Noyes, Jr., *ibid.*, **56**, 1305 (1934).
(27) R. D. Suart, Thesis, University of British Columbia, Vancouver, B. C.
(28) S. W. Benson and R. Shaw, to be submitted.

$k_{15'}$ may be estimated at $10^{9.2 - 4/\theta}$ (the A factor for addition should be $\sim 10^{10}$ so that addition at a particular site is $\sim 10^{10}/6 = 10^{9.2}$), with $(Cl_2) = 10^{-2.2}$ moles/l. Then

$$\text{rate}/(C_6H_5NO_2) \simeq 10^{-2.9} \text{ sec}^{-1}$$

In this case, NO_2 acts as a catalyst for establishing the Cl_2–Cl equilibrium.

Levine and Noyes[29] have studied the exchange of radioactive iodine with iodobenzene and *p*-nitroiodobenzene in solution (Y = I* and X = I). They found that exchange occurred by two paths, one of which was first order in aromatic and half-order in iodine. For this path they proposed a free-radical mechanism formally equivalent to that suggested here, so that

$$(\text{rate})_{ex} = 0.5k_{15'}K_{I_2}^{1/2}(C_6H_5I)(I_2)^{1/2}$$

The rate constant for exchange in the temperature range of 170–200° was

$$\log (k_{ex}, \text{l.}^{1/2} \text{mole}^{-1/2} \text{sec}^{-1}) = 10.5 - 35/\theta$$

so that

$$\log (k_{15'}, \text{l. mole}^{-1} \text{sec}^{-1}) = 9.13 - 17.3/\theta$$

The A factor for (15') is in good agreement with the estimate above, and $E_{15'}$ leads to a stabilization energy for the cyclohexadienyl radical of 25.5 kcal/mole, if $E_{16'} = 2$ kcal/mole.[30,31] This, too, is in good agreement with the chlorination data.

Reaction 19 would be expected to have a kinetic isotope effect of $k_{19}(H)/k_{19}(D) \cong 2$. The reported[24,32] value of 1.4 for benzene-1,3,5-d_3 is consistent with this mechanism, as is the isotope effect of about 1.5 for benzene and benzene-d_6.[32]

The detailed analysis of the isomeric distribution of the product would be very complex. However, qualitatively one would expect the distribution to be essentially temperature independent and statistical with the exception that *ortho* substitution might show a steric effect and be lower than expected (*ortho* substitution requires abstraction of a hydrogen atom in (19) adjacent to the X group). This is essentially consistent with the observations.[24,25,33] The nonstatistical *meta/ortho* ratio, generally about 4 to 6, suggests such a steric effect.

The addition mechanism is also consistent with the generally accepted reactions of free radicals with aromatic compounds[34] and has been shown to account for the kinetics of hydrogenation of toluene and xylene.[35]

Appendix

The rate constants k_{17} and k_{19} may be estimated from analogous reactions in the literature;[36,37] thus, on a per site basis

$$\log (k_{17}, \text{l. mole}^{-1} \text{sec}^{-1}) \sim 9.0 - 3/\theta$$

and

$$\log (k_{19}, \text{l. mole}^{-1} \text{sec}^{-1}) \sim 10 - 3/\theta$$

k_{18} may be taken similar to k_{19}.

The heat of reaction 15 is given by

$$\Delta H_{15,16}^\circ = D_\pi^\circ(A) + SE^\circ(C_6H_5X) - DH^\circ(C\text{–}Cl) - SE^\circ(B)$$

$$A = \langle\bigcirc\rangle, \quad B = \text{(structure)}\text{–}X$$
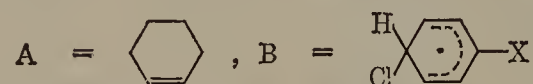
in which the π bond in benzene has been equated to the π bond in cyclohexene, $D_\pi^\circ(A)$, and $SE^\circ(C_6H_5X)$ and $SE^\circ(B)$ are the stabilization energies of benzene and the cyclohexadienyl radical, respectively.

To evaluate these quantities, it is assumed that the bond dissociation energy $DH^\circ(C\text{–}X)$ in cyclohexane is the same as in CH_3–CHX–CH_3. Therefore[38] $D_\pi^\circ{}_{298}$ (cyclohexene) = 56.4 kcal/mole, $DH^\circ{}_{298}(C\text{–}Cl) = 81.0$, and $SE^\circ{}_{298}$(benzene) = 36.5.

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(30) R. M. Noyes, R. G. Dickinson, and V. Schomaker, *ibid.*, **67**, 1319 (1945).
(31) S. W. Benson, K. W. Egger, and D. M. Golden, *ibid.*, **87**, 469 (1965).
(32) E. C. Kooyman, *Pure Appl. Chem.*, **7**, 193 (1963).
(33) J. W. Engelsma, E. C. Kooyman, and J. R. Van der Bij, *Rec. Trav. Chim.*, **76**, 325 (1957).
(34) See, for example, C. Walling, "Free Radicals in Solution," John Wiley and Sons, New York, N. Y., 1958: (a) p 156; (b) pp 308–310; (c) 482–485; (d) pp 496–497.
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(36) P. B. Ayscough, A. J. Cocker, F. S. Dainton, and S. Hearst, *Trans. Faraday Soc.*, **58**, 295 (1962).
(37) G. C. Fettis and J. H. Knox, *Progr. Reaction Kinetics*, **2**, 3 (1964).
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Reactions of the Carbonium Ions from the Decay of Propane-1,2-t_2 in Gaseous and Liquid Propane

Fulvio Cacace, Marcello Caroselli, and Angelo Guarino

Contribution from Centro Nazionale di Chimica delle Radiazioni e Radioelementi del C.N.R., Istituto di Chimica Farmaceutica dell' Università, Rome, Italy. Received March 28, 1967

Abstract: The chemical fate of a tritiated propane molecule following the decay of the radioactive atom has been studied with a tracer technique involving the use of propane-1,2-t_2. The isotopically pure compound was allowed to decay in the presence of a large excess of inactive propane, both in the gas phase at 1 atm and in the liquid phase at $-130°$. The analysis of the labeled decay products was carried out by radio gas chromatography. The results obtained were compared with the low-pressure, decay-induced fragmentation pattern of propane-1-t and propane-2-t. The results are consistent with the view that the dissociation process, $C_3H_7^+ = C_3H_5^+ + H_2$, of the excited daughter ions observed at 10^{-5} torr is largely prevented in the gas phase at 1 atm by collisional deactivation processes, as suggested by the low yields of molecular hydrogen and propylene. The stabilized $C_3H_6T^+$ ions react with the inactive propane to give monotritiated propane and unlabeled propyl ions, indicating a thermoneutral hydride ion transfer process. Those $C_3H_6T^+$ ions (20%) that receive from the nuclear decay a larger excitation energy fragment into smaller ions and give tritiated products other than propane. The nature and the yields of the labeled products observed are in good agreement with those expected, if one takes into account the low-pressure fragmentation pattern and the ion–molecule reactions that are known to occur within the system. In the liquid phase, the only major product observed is propylene, along with a smaller amount of molecular hydrogen. The product distribution suggests that, when the decay takes place in liquid propane, most of the daughter $C_3H_6T^+$ ions are stabilized. Even in those cases when the nuclear transition leaves the organic ion in a highly excited state, its dissociation is limited to the first step, *i.e.*, to the process $C_3H_6T^+ = C_3H_4T^+ + H_2$. The $C_3H_4T^+$ ion, reacting with the inactive propane, eventually give rise to tritiated propylene.

A detailed investigation on the chemical reactions following the β decay of a tritium atom contained, respectively, in the molecules of methane and ethane has been carried out by means of a tracer technique involving the use of multilabeled alkanes.[1-3] The present paper describes the extension of the investigation to the chemical processes promoted by the decay of a radioactive atom contained in propane-1,2-t_2.

The choice of this molecule was suggested by the following considerations. In the first place, the necessary data on the low-pressure, decay-induced fragmentation of propane-1-t and propane-2-t had been determined by Wexler, Anderson, and Singer[4] with a specially designed mass spectrometer.

Secondly, the reactions of many organic ions in gaseous propane are well known, as a consequence of extensive investigations carried out with high-pressure mass spectrometric methods. Furthermore, the boiling point of propane makes it convenient to store, even for extended periods of time, samples of liquid $C_3H_6T_2$, thus allowing the study of the decay-promoted reactions not only in the gas but also in the liquid phase.

Finally, a study of the chemical reactions promoted by the decay of propane-1,2-t_2 is of special interest, in view of the unique fragmentation pattern determined by the low-pressure decay of propane-1-t and propane-2-t, which shows a significant deviation from those observed in the decay of all the other tritiated hydrocarbons so far investigated.[4-7]

In particular, the yields of the initial fragment, *i.e.*, the $C_3H_7^+$ ion, from the decay of propane-1-t and propane-2-t are 56 and 41%, respectively. This is to be compared with the much higher yields of the initial fragment from the decay of CH_3T, C_2H_5T, C_6H_5T, and the four monotritiated toluenes, all of which range from 83 to 72%. The relatively high percentage of daughter ions that dissociate, following the decay of both the monotritiated propanes at 10^{-5} torr, is not determined, according to Wexler,[4] by an unusually high amount of excitation energy imparted to the ion by the nuclear transition. The observed fragmentation is rather produced by the facile decomposition of the $C_3H_7^+$ ions into $C_3H_5^+$ ions, requiring only 4–10 kcal/mole for the primary and 30–40 kcal/mole for the secondary propyl ions.[4]

While this suggestion is quite reasonable, from the low-pressure fragmentation data it can only be inferred that in the decay of propane-1-t and propane-2-t a considerable fraction of the $C_3H_7^+$ ions is formed in states of excitation energy comprised between 4–14 kcal/mole and, say, 100 kcal/mole. The lower limit is set by the energy required to form a $C_3H_5^+$ ion from a primary $C_3H_7^+$ ion, while the upper limit represents the energy required for the next step of unimolecular decomposition, involving a more extensive fragmentation, for instance, the formation of $C_3H_3^+$ or $C_2H_3^+$ ions.

It was hoped that the present experiments, involving the decay of propane-1,2-t_2 at 760 torr and in the liquid phase, *i.e.*, in systems where the stabilization of the excited ions becomes increasingly effective, could be useful, *inter alia*, to provide additional information on

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(2) B. Alipranti, F. Cacace, and A. Guarino, *J. Chem. Soc., Sect. B*, 519 (1967).

(3) F. Cacace, presented at the 152nd National Meeting of the American Chemical Society, New York, N. Y., Sept 1966.

(4) S. Wexler, G. R. Anderson, and L. A. Singer, *J. Chem. Phys.*, **32**, 417 (1960).

(5) A. H. Snell and F. Pleasonton, *J. Phys. Chem.*, **62**, 1377 (1958).

(6) S. Wexler and D. C. Hess, *ibid.*, **62**, 1382 (1958).

(7) T. A. Carlson, *J. Chem. Phys.*, **32**, 1234 (1960).

the excitation level of those propyl ions that were found to dissociate into $C_3H_5^+$ ions at 10^{-5} torr.

Experimental Section

Materials. Propane-1,2-t_2 was obtained from propylene by reaction with tritium gas over a chromia–gel catalyst prepared and activated according to Burwell, et al.[8] Undesirable hydrogen exchange and double-bond migration reactions were found by these authors to be slow in comparison with the hydrogenation itself, as demonstrated by the high isotopic purity of the resulting deuterated hydrocarbons.

Propylene (0.033 mmole) and tritium gas (4 curies) were allowed to react in the presence of chromium oxide (40 mg) at $-12°$ for a period of 36 hr. A large excess of inactive propane was immediately added to the reaction mixture, and most of the unreacted T_2 was eliminated by freezing and outgassing the sample.

The crude labeled propane was then purified twice by preparative gas chromatography, using a 4-m column, heated to $100°$ and packed with activated silica gel. After the second purification step, a radio gas chromatographic analysis of the propane failed to detect active impurities.

Unlike the tritiated methanes, the various propanes containing a different number of tritium atoms cannot be separated by gas chromatography. Therefore, a mass spectrometric analysis of the purified labeled propane was carried out. The percentage of monotritiated propane, the most likely impurity, was found to be below the detection limit, estimated to be around 10%. More significantly, the abundance of propane-1,2-t_2, i.e., the ratio $C_3H_6T_2/C_3H_8$, was found to be in excellent agreement with the value calculated from a measurement of the specific activity of the sample.

The purified propane-1,2-t_2 was further diluted to the desired specific activity with inactive propane before being stored for the growth of the decay products.

The propylene, propane, and the other hydrocarbons used as carriers were commercial (Rivoira S.p.A., Torino) samples with a purity greater than 99.9%. The tritium gas was obtained from CEA (France) and its stated purity was greater than 95%, the main contaminant being ^3He. A gas chromatographic analysis carried out according to Smith and Carter[9] showed that the HT content in the sample was lower than 2%.

Growth and Analysis of the Decay Products. The propane-1,2-t_2 was allowed to decay in propane + 0.5% O_2 at room temperature and 1 atm for a period of 4 weeks. The samples were stored in 100-ml Pyrex ampoules and their specific activity was kept between 0.5 and 1 mcurie per mmole of gas. The propane-1,2-t_2 was also allowed to decay in liquid propane (both neat and containing 2% O_2) at $-130°$ for the same period of time.

The analysis of the labeled decay products was carried out by radio gas chromatography, using a flow ionization chamber and a vibrating reed electrometer, according to a technique already described.[10] The following columns were employed for the analysis of the tritiated hydrocarbons: a 4-m column packed with activated silica gel and heated to $100°$ was used for the separation of $(H_2 + CH_4)$, C_2H_6, C_2H_4, C_3H_8, and C_3H_6; a 3-m column packed with 5-A molecular sieves and heated to $100°$ was employed for the separation of H_2 from CH_4; a 2-m column of activated alumina, coated with 0.5% of silicone oil, purchased from the Burrell Co. (Pittsburgh, Pa.), was used for the separation of the C_3 and the C_4 hydrocarbons; a 12-m dimethylsulfolane column was chosen to separate $(H_2 + CH_4)$, $(C_2H_4 + C_2H_6)$, propylene, propane, and acetylene.

Results and Discussion

The yields of the tritiated products from the decay of propane-1,2-t_2 in the systems investigated are given in Table I. These yields represent the per cent of activity of the labeled fragments from the decay of $C_3H_6T_2$, i.e., of the $C_3H_6T^3He^+$ ions, which is contained in each of the products identified.

Effects of the Radiation Damage to the System. The self-radiolysis of the sample, caused by the β

(8) R. L. Burwell, Jr., et al., J. Am. Chem. Soc., **82**, 6272 (1960).
(9) H. A. Smith and E. H. Carter, "Tritium in the Physical and Biological Sciences," Vol. I, International Atomic Energy Agency, Vienna, 1962, p 121.
(10) F. Cacace, Nucleonics, **19**, 5, 45 (1961).

Table I. Yields of Labeled Products from the Decay of Propane-1,2-t_2 in Propane

| Product | Yields[a] | | |
	Propane + 2% O_2 gas phase at 25°	Propane + 2% O_2[b] liquid phase at −130°	Propane liquid phase at −130°
HT	9.3	4.4	5.3
CH_3T	7.9	2.2	2.4
C_2H_5T	1.9	1.0	1.1
C_2H_3T	4.9	1.8	1.8
C_2HT	0.7	2.7	2.7
C_3H_5T[c]	6.0	13.8	12.4
C_3H_3T[d]	~4.9[e]	1.8[e]	1.8[e]
C_4H_9T	...	...	...

[a] Percentage of the total activity of the $C_3H_6T^3He^+$ decay fragments found in each product. The standard deviation of the data is below 10%. [b] This value represents the percentage of oxygen added to propane before the condensation at −130°. [c] Propylene. [d] Allene + methylacetylene. [e] Approximate value owing to incomplete gas chromatographic separation.

particles associated with the decay of $C_3H_6T_2$, promotes the formation of labeled compounds, which could superimpose a product spectrum on the tritiated substances arising from the reactions of the $C_3H_6T^3He^+$ ions. The specific activity of the samples was therefore kept to the lowest level compatible with the requirements of the radiometric analysis. In the reasonable hypothesis that the G_{-M} value[11] is the same for propane and propane-t_2, one can calculate an upper limit for the yield of labeled products formed by radiolytic processes during the storage of samples having a specific activity below 0.5 mcurie/mmole. The results show that the activity of the radiolytic products is quite small when compared to the activity of the $C_3H_6T^3He^+$ ions formed in the same storage period. These estimates have been fully verified by blanks carried out with monotritiated methane and ethane in the study of the methane-t_4 and ethane-1,2-t_2 decay, respectively.[1–3]

These and other considerations, including the observation that the combined activity of the products identified is invariably smaller than the activity contained in the primary decay fragments and the minor effect of the radical scavengers on the product distribution, make it reasonable to assume that the tritiated products listed in Table I are formed by the reactions of the $C_3H_6T^3He^+$ ions with no significant contribution from radiolytic processes.

Decay-Induced Fragmentation of Propane-1,2-t_2. Since the probability of a decay event is independent of the position of the radioactive atom in the molecule, the propane-1,2-t_2 can be regarded, from the point of view of the fragmentation following the decay, as an equimolecular mixture of propane-1-t and propane-2-t. The resulting fragmentation pattern can be calculated from the data of Wexler and is given in Table II. The excess of inactive propane contained in the system intercepts any undissociated $C_3H_6T^+$ ion formed in the β decay, according to the thermoneutral hydride ion transfer reaction
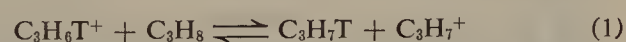
$$C_3H_6T^+ + C_3H_8 \rightleftharpoons C_3H_7T + C_3H_7^+ \qquad (1)$$

(11) A. J. Swallow, "Radiation Chemistry of Organic Compounds," Pergamon Press, London, 1960, p 64.

The product of reaction 1, which has been established by Pettersson and Lindholm,[12] by Aquilanti and Volpi,[13] and by Sieck and Futrell[14] with deuterated reagents, is monotritiated propane, which cannot be detected in the presence of the excess of propane-1,2-t_2 necessary to produce the labeled decay fragments.

Table II. Low-Pressure Fragmentation of an Equimolecular Mixture of Propane-1-t and Propane-2-t Following β Decay[a]

m/e	Ionic fragment	Abundance, %
46	$(C_3H_7{}^3He)^+ +$ $C_3H_7T^+$	<0.2
43	$C_3H_7{}^+$	48.50 ± 0.90
42	$C_3H_6{}^+$	2.80 ± 0.30
41	$C_3H_5{}^+$	18.00 ± 1.00
40	$C_3H_4{}^+$	0.90 ± 0.10
39	$C_3H_3{}^+$	4.60 ± 0.40
38	$C_3H_2{}^+$	3.50 ± 0.30
37	C_3H^+	3.60 ± 0.30
36	$C_3{}^+$	1.10 ± 0.10
29	$C_2H_5{}^+$	1.18 ± 0.30
28	$C_2H_4{}^+$	0.60 ± 0.10
27	$C_2H_3{}^+$	5.10 ± 0.70
26	$C_2H_2{}^+$	3.40 ± 0.30
25	C_2H^+	1.40 ± 0.20
24	$C_2{}^+$	0.60 ± 0.10
15	$CH_3{}^+$	1.40 ± 0.20
14	$CH_2{}^+$	0.80 ± 0.10
13	CH^+	0.55 ± 0.07
12	C^+	0.50 ± 0.07
3	$(^3He)^+$	<0.1
2	H^{2+}	<0.1
1	H^+	0.80 ± 0.10
20.5	$C_3H_5{}^{2+}$	0.15 ± 0.10
20.0	$C_3H_4{}^{2+}$	0.40 ± 0.10
19.5	$C_3H_3{}^{2+}$	0.20 ± 0.10
19.0	$C_3H_2{}^{2+}$	0.80 ± 0.20

[a] Calculated from ref 4; see text.

The over-all effect of reaction 1 would be simply to decrease the fraction of the activity contained in the observable labeled products. Therefore, it is possible to use the combined yields of the tritiated hydrocarbons identified as an indirect criterion to establish the abundance of the undissociated $C_3H_6T^+$ ions formed when the decay takes place in propane at 1 atm or in liquid propane.

Decay in the Gas Phase. In the gas phase, the total activity contained in products other than propane is 34.9%, in comparison with the value of 51.5% calculated from the data of Table II using the hypothesis that the decay-induced fragmentation processes are independent of pressure, as found in the decay of ethane-t_2 and methane-t_4.

This result, while hardly conclusive, suggests however that the fraction of $C_3H_6T^+$ ions escaping dissociation is higher than in the low-pressure experiments.

The most abundant fragment at low pressure is the $C_3H_4T^+$ ion, produced in 18% of the nuclear transitions. Such an ion reacts with propane according to the well-established[15] hydride ion transfer process 2, to produce labeled propylene. The observed propylene yield,

$$C_3H_4T^+ + C_3H_8 \longrightarrow C_3H_5T + C_3H_7{}^+ \qquad (2)$$

(12) E. Pettersson and E. Lindholm, *Arkiv Fysik*, **24**, 49 (1963).
(13) V. Aquilanti and G. G. Volpi, *J. Chem. Phys.*, **44**, 2307 (1966).
(14) L. W. Sieck and J. H. Futrell, *ibid.*, **45**, 560 (1966).
(15) G. A. W. Derwish, A. Galli, A. Giardini-Guidoni, and G. G. Volpi, *ibid.*, **41**, 2998 (1964).

including the contributions from the reactions of the other ions, is only one-third of the value expected from the data of Table II. This may be taken as strong evidence that a substantially smaller fraction of the decay-formed, excited $C_3H_6T^+$ ions dissociate at atmospheric pressure to give $C_3H_4T^+$ ions.

On the other hand, the formation of tritiated products other than C_3H_7T, including HT, CH_3T, C_2H_5T, etc., with a total yield of about 30%, indicates that a corresponding aliquot of the $C_3H_6T^+$ ions fragmentate, even when the decay occurs at atmospheric pressure. For instance, the yield of C_2H_3T, formed from the $C_2H_2T^+$ ions *via* a hydride ion transfer from propane, approaches the value expected on the basis of the low-pressure fragmentation data.

The high efficiency of the stabilization process which prevents, at 760 torr, the fragmentation of that fraction of $C_3H_6T^+$ ions that would dissociate into $C_3H_4T^+$ ions at 10^{-5} torr is to be compared with the lack of a measurable stabilization for those $C_3H_6T^+$ ions that undergo a more extensive fragmentation at low pressure.

The comparison suggests that the excitation level of those $C_3H_7{}^+$ ions that have been found to produce $C_3H_5{}^+$ ions at 10^{-5} torr is low indeed, as suggested by Wexler,[4,16] and actually approaches the inferior limit of the large energy interval allowed by his mass spectrometric experiments.

We shall therefore assume, in agreement with the theoretical model on the molecular excitation following the β decay, that the excitation energy of 70 to 80% of the organic ions produced by the nuclear transition is sufficiently low and distributed in such a way as to make their collisional stabilization possible at 760 torr. The remaining 20% or so of the organic ions is formed in higher excited states (up to 20 ev), and the distribution of excitation energy is such as to make their stabilization impossible even at 1 atm pressure.

Therefore, the data of Wexler[4] on the abundance of the fragments from the highly excited $C_3H_7{}^+$ ions from the nuclear decay will be directly employed to evaluate the nature and the yields of the labeled products other than propane.

Table III summarizes the yields of the tritiated products (HT, CH_3T, etc.) from the primary dissociation of the highly excited $C_3H_6T^+$ ions, calculated by making reasonable hypotheses on the nature of the neutral fragments arising from any dissociation process. In view of the lack of more detailed information, it has been assumed that the tritium activity is distributed in a statistical way among the reaction products.

In addition to the stable products from reactions 3 to 18 (Table III), other products arise from the reactions of the tritiated ions with propane. The reactions of several ions ($C_3H_5T^+$, $C_3H_3T^+$, C_3HT^+, C_3T^+, etc.) are not known. The other ions react according to the well-established processes 19 to 25, to give products whose calculated yields are summarized in Table IV.

In order to calculate the over-all yield of a given product, the contributions from the pertinent processes listed in Tables III and IV are combined. The calculated product distribution shows a satisfactory agreement with the experimental yields (Table V), with the exception of the propylene and the C_3H_4 hydrocarbons.

(16) S. Wexler, "Actions Chimiques et Biologiques des Radiations," Vol. 8, M. Haissinsky, Ed., Masson et Cie, Paris, 1965, p 143.

Table III. Labeled Products Formed from the Primary Fragmentation Following the Decay of Propane-1,2-t_2 in Gaseous Propane

Dissociation reaction[a]	Calculated yield[b] of tritiated products, %			
(3) $C_3H_6T^+ \rightarrow C_3H_4^{*+} + H_2^* + H^*$	HT	0.3		
(4) $C_3H_6T^+ \rightarrow C_3H_3^{*+} + 2H_2^*$	HT	2.6		
(5) $C_3H_6T^+ \rightarrow C_3H_2^{*+} + 2H_2^* + H^*$	HT	2.0		
(6) $C_3H_6T^+ \rightarrow C_3H^{*+} + 3H_2^*$	HT	3.1		
(7) $C_3H_6T^+ \rightarrow C_3^+ + 3H_2^* + H^*$	HT	0.9		
(8) $C_3H_6T^+ \rightarrow C_2H_5^{*+} + CH_2^*$	...	...		
(9) $C_3H_6T^+ \rightarrow C_2H_4^{*+} + CH_3^*$	...	...		
(10) $C_3H_6T^+ \rightarrow C_2H_3^{*+} + CH_4^*$	CH_3T	2.9		
(11) $C_3H_6T^+ \rightarrow C_2H_2^{*+} + CH_4^* + H^*$	CH_3T	1.9		
(12) $C_3H_6T^+ \rightarrow C_2H^{*+} + CH_4^* + H_2^*$	HT	0.4	CH_3T	0.8
(13) $C_3H_6T^+ \rightarrow C_2^+ + CH_4^* + H_2^* + H^*$	HT	0.2	CH_3T	0.3
(14) $C_3H_6T^+ \rightarrow CH_3^{*+} + C_2H_4^*$	C_2H_3T	0.8		
(15) $C_3H_6T^+ \rightarrow CH_2^{*+} + C_2H_4^* + H^*$	C_2H_3T	0.5		
(16) $C_3H_6T^+ \rightarrow CH^{*+} + C_2H_4^* + H_2^*$	C_2H_3T	0.3	HT	0.2
(17) $C_3H_6T^+ \rightarrow C^+ + C_2H_4^+ + H_2^* + H^*$	C_2H_3T	0.3	HT	0.1
(18) $C_3H_6T^+ \rightarrow H^+ + C_3H_6^*$	$C_3H_5T^c$	0.7		

[a] The asterisk indicates a tritiated species, containing a statistical fraction of the activity initially present in the $C_3H_6T^+$ ion. [b] See footnote a of Table I. [c] Propylene.

Table IV. Labeled Products from the Reactions of Tritiated Primary Ions with Propane

Reaction	Calculated yield of the tritiated product, %	
(19) $C_3H_2T^+ + C_3H_8 \rightarrow C_3H_3T + C_3H_7^{+\,a}$	$C_3H_3T^d$	2.0
(20) $C_2H_4T^+ + C_3H_8 \rightarrow C_2H_5T + C_3H_7^{+\,b}$	C_2H_5T	1.3
(21) $C_2H_3T^+ + C_3H_8 \rightarrow C_2H_5T + C_3H_6^{+\,b}$	C_2H_5T	0.3
(22) $C_2H_2T^+ + C_3H_8 \rightarrow C_2H_3T + C_3H_7^{+\,a-c}$	C_2H_3T	2.2
(23) $C_2HT^+ + C_3H_8 \rightarrow C_2HT + C_3H_8^{+\,a}$	C_2HT	1.0
(24) $CH_2T^+ + C_3H_8 \rightarrow CH_3T + C_3H_7^{+\,c}$	CH_3T	0.6
(25) $C_3H_3T^+ + C_3H_8 \rightarrow C_3H_5T + C_3H_6^+$	$C_3H_5T^e$	0.5

[a] Reference 15. [b] M. S. B. Munson and F. H. Field, *J. Am. Chem. Soc.*, **87**, 3294 (1965). [c] Reference 12. [d] Allene + methylacetylene. [e] Propylene.

Table V. Comparison of Calculated and Experimental Yields of Labeled Products from the Decay of Gaseous Propane

Product	Yield, %	
	Calcd[a]	Found
HT	9.8	9.3
CH_3T	6.5	7.9
C_2H_5T	1.6	1.9
C_2H_3T	4.1	4.9
C_2HT	1.0	0.7
$C_3H_5T^b$	1.2	6.0
$C_3H_3T^c$	2.0	4.9
C_4H_9T	...	...
Total activity in products other than C_3H_7T	33.5[d]	35.6

[a] See text. [b] Propylene. [c] Allene + methylacetylene. [d] Calculated from the abundance of propyl + propylene ions given in Table I.

It should be pointed out, however, that the calculated yields represent at best *a lower limit*, since the reactions of several tritiated ions, *i.e.*, the $C_3H_5T^+$, $C_3H_3T^+$, C_3HT^+, C_3T^+, CHT^+, and CT^+ ions, whose combined activity reaches about 5%, are not known and have not been considered. In addition, the isotope effects and the possibility of a nonstatistical tritium distribution can effect, to some extent, the calculated distribution.

Decay in the Liquid Phase. The yields of the tritiated products show a dramatic change when the decay takes place in liquid propane at $-130°$. First, the HT yield, which provides a rough indication of the extent of the primary fragmentation processes, drops to less than one-half of the value found in gas-phase decay, while the tritiated propylene yield is more than doubled, in contrast with the sharply reduced yields of all the other products. Both these findings can be rationalized if one assumes that the much shorter time required for collision in the liquid phase tends to stabilize all the $C_3H_6T^+$ ions formed in lower excitation states, including part of those ions that would dissociate in the gas phase at 760 torr. The stabilized ions react with the inactive propane to give monotritiated propane according to reaction 1.

In addition, even in those cases where the fast dissociation of highly excited $C_3H_6T^+$ ions takes place, the chain of unimolecular fragmentation processes that could lead to extensively "degraded" ions is limited to the first step, *i.e.*, the formation of the $C_3H_4T^+$ ion. Such a species, stabilized by collision, eventually reacts with the inactive propane to form C_3H_5T through the hydride ion transfer process (eq 2).

Only a minor fraction of the β transitions, where the daughter ions are formed with an extremely high excitation energy, lead to such products as labeled methane, acetylene, and ethylene. The yield of these latter products in the liquid propane is, in any case, much lower than in the gas phase.

Conclusions

The analysis of the tritiated products from the decay of propane-1,2-t_2 in gaseous propane at 760 torr indicates that even in the case of propane, as for the other alkanes so far investigated, 70 to 80% of the nuclear transitions produce daughter ions in states of low excitation energy. All these ions survive fragmentation when the decay occurs at atmospheric pressure and react with the inactive propane forming C_3H_7T. The remaining 20–30% of the β transitions produces highly excited ions, which are not stabilized even at atmospheric pressure and fragment into smaller ions. Such dissociation and the reactions of the fragment ions are responsible for the formation of the labeled products other than C_3H_7T.

The general interpretation of the product distribution from the decay in the gas phase is confirmed by the results obtained from the decay in liquid propane.

Here the dissociation of the daughter $C_3H_5T^+$ ions is largely prevented. When the dissociation takes place, it is limited to its first step involving the formation of $C_3H_4T^+$ ions, which react with inactive propane to give C_3H_5T, the major product observed.

Flash Photolysis Studies of 1,3,5-Cyclooctatriene. A Reversible Ring Opening[1a,b]

Theodore D. Goldfarb[2] and Lars Lindqvist

Contribution from the Laboratoire de Chimie Physique, Faculté des Sciences, Orsay, France. Received March 31, 1967

Abstract: Studies of 1,3,5-cyclooctatriene in cyclohexane and *n*-hexane by flash photolysis have resulted in the detection of two transient species, both of which decay by first-order processes with lifetimes (at 25° in *n*-hexane) of 91 msec and 23 sec. Both transients are formed during the flash. A fivefold increase in the concentration of the long-lived species occurs simultaneously with the disappearance of the short-lived species. From spectroscopic and kinetic evidence the long-lived species is identified as *cis,cis*-1,3,5,7-octatetraene, the instability of which results from a low activation energy (17 kcal/mole) for recyclization to 1,3,5-cyclooctatriene. Arguments are presented for the identification of the short-lived transient as a strained, cyclic stereoisomer of 1,3,5-cyclooctatriene. The opening of this cyclic transient to form octatetraene has an Arrhenius activation energy of 16 kcal/mole. The formation of stable 1,3,5,7-octatetraene (*cis,trans* and/or *trans,trans*) has been observed and has been found to occur *via* the photoisomerization of the unstable *cis,cis* stereoisomer, thus providing an example of a biphotonic process.

There has been much recent interest in the photochemistry of cyclic polyenes. Numerous rearrangement reactions have been investigated yielding results of considerable importance from a mechanistic point of view.[3] Although one would expect that transient as well as stable photoisomers might be involved in the photochemical rearrangements of these molecules, previous work has been directed almost exclusively toward observing the stable products. In an attempt to detect and characterize transient species, we have applied the flash photolysis technique to the study of a representative compound, 1,3,5-cyclooctatriene (I). Previous photochemical studies[4-6] have shown that prolonged photolysis of I in a variety of solvents produces a bicyclic isomer (II) as well as a tricyclic isomer (III). These results differ markedly from those reported

II   III
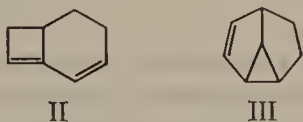
for 1,3-cyclohexadiene for which the primary photochemical process in solution[7a] is ring opening to 1,3,5-

hexatriene. As suggested by Barton,[7b] a ring with $2n$ members containing $n - 1$ conjugated double bonds should undergo facile photochemical conversion to an open chain compound with n conjugated double bonds. The failure of previous workers[4-6] to isolate 1,3,5,7-octatetraene as a major photolysis product of I is shown by the present results to be due to the unexpected rapidity with which the *cis,cis* isomer of this conjugated polyene recyclizes to I. Evidence will also be presented for the identification of a second important transient as a photochemically produced stereoisomer of I.

Experimental Section

The flash photolysis apparatus consists of six oxygen-filled quartz discharge tubes, each 20 cm long, capable of producing flashes with a total discharge energy of 3750 joules and a duration of 4 μsec.[8] Solutions to be studied were contained in a jacketed 20-cm quartz cell. The filter jacket was filled with distilled water during all runs except for one experiment using a glacial acetic acid filter as described below.

Transient changes in optical density following a flash were followed by employing a d.c. xenon lamp (Osram XBO 150 W/1), a grating monochromator (Bausch and Lomb f/4.4 0.5M) adjusted for 1-mμ band width, a photomultiplier tube (EMI 955 8 BQ), and an oscilloscope (Tektronix 535) fitted with a Polaroid camera in the standard manner.

I was synthesized, purified, and separated from its thermal bicyclic isomer according to the procedure described by Cope, *et al.*[9]

Transient optical density changes were measured over the 250–500-mμ wavelength range at intervals of 20 mμ after flashing solutions of I in Spectrograde cyclohexane (1–30 $\times$ 10^{-6} *M*). The region where a positive result was obtained was reinvestigated at intervals of 2–3 mμ.

(1) (a) This work was supported in part by the AFOSR (SRC)-OAR USAF under grant No. 837-65; (b) presented in part at the 153rd National Meeting of the American Chemical Society, Miami Beach, Fla., April 1967.

(2) To whom inquiries should be addressed at the Department of Chemistry, State University of New York, Stony Brook, N. Y. 11790.

(3) See, for example, the recent article by R. N. Warrener and J. B. Bremner, *Rev. Pure Appl. Chem.*, **16**, 117 (1966).

(4) O. L. Chapman, G. W. Borden, R. W. King, and B. Winkler, *J. Am. Chem. Soc.*, **86**, 2660 (1964).

(5) J. Zirner and S. Winstein, *Proc. Chem. Soc.*, 235 (1964).

(6) W. R. Roth and B. Peltzer, *Angew. Chem.*, **76**, 378 (1964).

(7) (a) The results of these studies are summarized in the recent review article by R. Srinivasan, *Advan. Photochem.*, **4**, 128 (1966); (b) D. H. R. Barton, *Helv. Chim. Acta*, **42**, 2604 (1959).

(8) A detailed description of this apparatus is presently being prepared for publication by L. L.

(9) A. C. Cope, A. C. Haven, F. L. Ramp, and E. R. Trumbal, *J. Am. Chem. Soc.*, **74**, 4867 (1952).
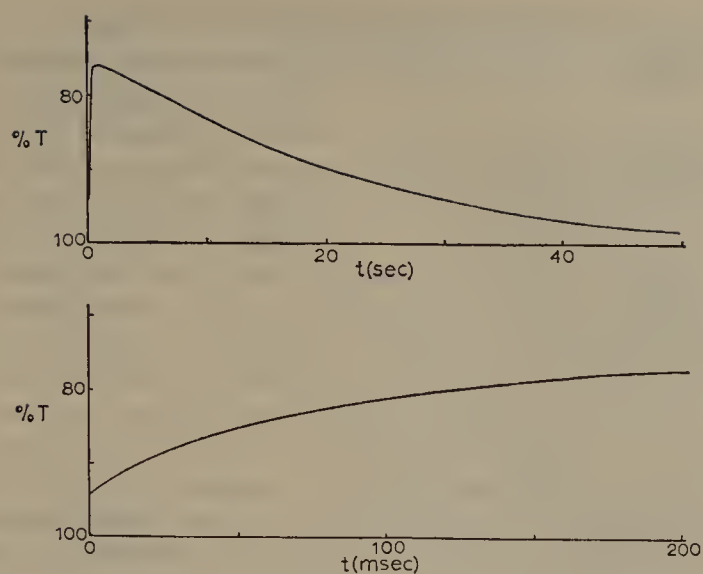
Figure 1. Enlarged oscilloscope traces of the change in transmittance, T, as a function of time, t, at slow (upper curve) and fast (lower curve) sweep rates.

Figure 2. Difference spectra: ΔD_m, $\bigcirc$; ΔD_M, $\times$. Spectrum of 1,3,5-cyclooctatriene, $\triangle$.

Data for Arrhenius plots were obtained with solutions maintained at fixed temperatures (to $\pm 0.1°$) over the range 9.9–50.0° by flowing water from a thermostatically controlled bath through the filter jacket of the cell. Spectrograde n-hexane was used as the solvent in these measurements.

Results

At low flash intensities (less than 500 joules discharge energy) a reversible change in optical density was observed at all wavelengths from 248 to 320 mμ for solutions of I (absorption maximum at 254 mμ) in cyclohexane or n-hexane. At higher light outputs the transmittance change was not completely reversible. Experiments in which glacial acetic acid (which cuts off the shorter wavelength half of the absorption band of I) was used as a filter gave qualitatively identical results with those obtained with a water filter. The same results were obtained using either thoroughly degassed or air-saturated solutions. The kinetics of the optical density changes observed were independent of concentration over the range studied (1×10^{-6}–3×10^{-5} M).

Figure 1 presents two typical oscillograms taken with the monochromator set at 295 mμ at sweep rates of 5 (upper curve) and 0.02 sec/cm (lower curve) following the low-intensity flashing of a 1.4×10^{-5} M solution of I in cyclohexane at 25°. The light transmitted by the solution before the flash is indicated as 100% on the ordinate scale. Immediately following the flash (the time resolution was about 20 μsec) a 6% drop in transmittance was observed, followed by an additional 18% decrease occurring over a period of about 0.2 sec. The transmittance then increased slowly approaching the original level. After 120 sec no additional changes were detected. Results of this general character were observed over the 250–320-mμ wavelength interval, clearly revealing the formation of two intermediate products, one with a short lifetime (X) and one with a longer lifetime (Y). Under the conditions of this experiment the permanent decomposition of I in a single flash was about 1% as measured both from spectra of the solution taken before and after a series of flash exposures as well as from the gradual decrease in the transient optical density changes following repetitive flashing. The products of this slight decomposition produced no detectable new absorption at wavelengths
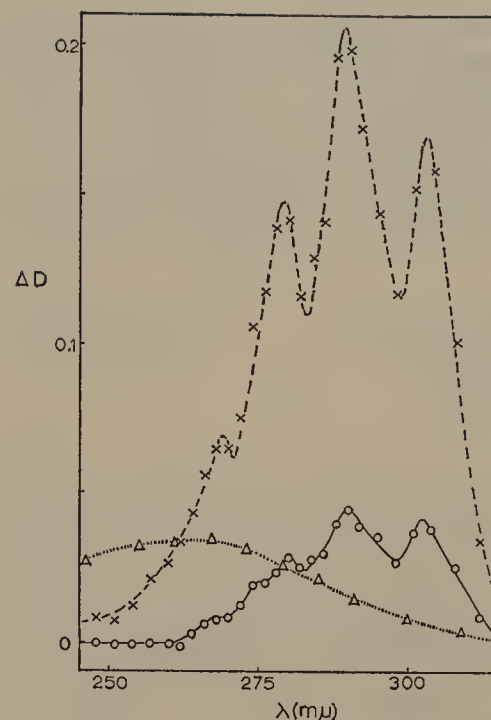
greater than 220 mμ. At higher flash energies a considerable increase in the transient effect was achieved but only at the expense of a larger decomposition of I accompanied by the appearance of a permanent absorption which was readily identified from its published spectrum[10,11] as being due to the formation of 1,3,5,7-octatetraene. The production of octatetraene went up very rapidly with increasing flash intensity, indicating that a biphotonic process was responsible for its formation. Because of the rapid onset of this two-photon side reaction it was necessary to measure the spectra of the transient species and to determine the effect of temperature on the decay rates at flash energies that were much below those required to achieve light saturation.

The spectral curves (difference spectra) shown in Figure 2 were constructed from the transient absorption changes for 1.1×10^{-5} M solutions of I in cyclohexane. The solid curve represents the observed changes in optical density (ΔD_m) immediately following the flash. The dashed curve is a plot of the decrease in optical density (ΔD_M) reached after the decay of X was virtually complete which corresponds to the difference between 100% and the minimum transmittance value on the oscillogram shown in Figure 1.

The ΔD_M values result from the increase in optical density due to the absorption of transient species Y modified by the decrease in optical density due to the decomposition (temporary and/or germanent) of I. The maxima in the dashed curve agree within experimental error (± 1 mμ) with both the published λ_{max} values of the stable stereoisomers of 1,3,5,7-octatetraene[10,11] and those observed for the permanent product produced by flashing at high light intensities. Assuming that the maximum extinction coefficient of Y is approximately the same as that of stable cis,trans-1,3,5,7-octatetraene[11] (see Discussion section for a justification of this assumption), it is estimated that about 4% of I was converted to Y under the conditions used in these runs. The absorption spectrum of a 20-

(10) G. F. Woods and L. H. Schwartzman, *J. Am. Chem. Soc.*, **71**, 1396 (1949).
(11) W. Ziegenbein, *Chem. Ber.*, **98**, 1427 (1965).
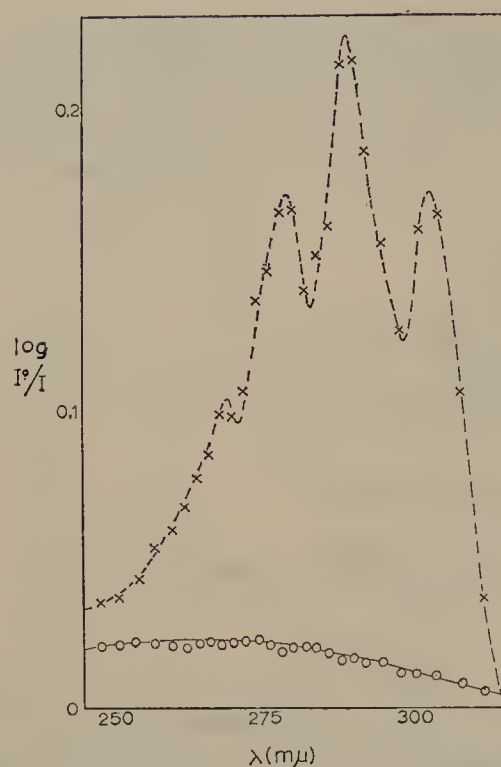
Figure 3. Calculated spectra: species X, ○; species Y, ✕.

Figure 4. Plots of lifetime ($-\log k$) vs. T^{-1} for species X, ✕, and for species Y, ○.

cm path length of a 4.4×10^{-7} M solution of I (4% of the original concentration) is shown by the dotted curve in Figure 2. Adding the dashed and dotted curves of Figure 2 should yield the undistorted spectrum of Y which is shown by the dashed curve in Figure 3.

The absorption peaks in the ΔD_m difference spectrum (solid curve in Figure 2) are seen to coincide in wavelength and relative intensity with those of Y, and it must therefore be assumed that some Y (about 20% of the total Y produced) has been formed during the flash, the remainder being formed from the short-lived transient, X. If it is assumed that all of the X formed is converted to Y, it is possible to construct an approximate spectrum of X by subtracting 20% of the dashed curve in Figure 3 from the solid curve in Figure 2, thus cancelling the effect of Y produced during the flash, and adding to this the dotted curve in Figure 2 in order to correct for the 4% decrease in the concentration of I. The result of this procedure is the solid curve in Figure 3. If some X reverts directly to I (the only other alternative consistent with the reversible nature of the photolytic process), the spectrum of X calculated by the above procedure should be modified by adding to it an additional fraction of the spectrum of I. In any event, species X is found to have a broad unstructured near-ultraviolet absorption band comparable in intensity to that of I but shifted to somewhat longer wavelengths. This latter point was verified by an experiment performed on a more concentrated sample (3×10^{-5} M) in which it was possible to observe transient changes at wavelengths as long as 324 mμ. Above about 318 mμ the increase in optical density immediately following the flash was followed by a *decrease* in absorbance with kinetics appropriate to the X → Y conversion process. This means that in this region X, although absorbing only weakly, has a higher extinction coefficient than either I or Y.

The difference in lifetime of species X and Y is large enough so that good kinetic data could easily be obtained from both the conversion of X to Y and for the disappearance of Y. A first-order decay was found for both processes at all concentrations, wavelengths, and temperatures studied. Arrhenius plots based on data taken at 10° intervals from 10 to 50° are shown in Figure 4. The values of the Arrhenius parameters for the decay of species X and Y are $A = 9.0 \times 10^{12}$ and 1.1×10^{11} sec^{-1} and $E_a = 16.3$ and 17.0 kcal/mole, respectively.
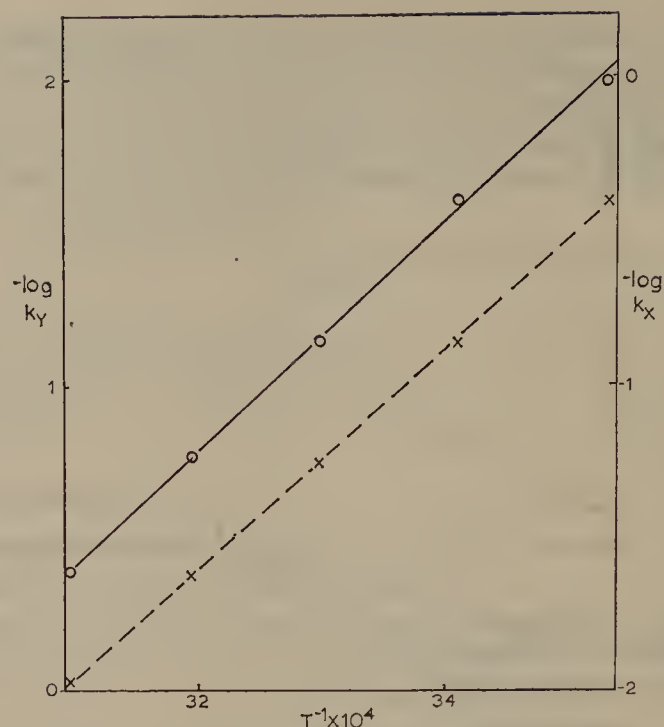
A few experiments were performed to investigate the nature of the biphotonic process which resulted in the irreversible conversion of I to 1,3,5,7-octatetraene. It seemed probable that photolysis of one or both of the transients was involved. To study the photolysis of Y, a solution of I in *n*-hexane (1.5×10^{-5} M), cooled to $-10°$, was exposed to two low-energy flashes spaced 15 sec apart. Only a very small fraction of the Y produced by the first flash had decayed prior to the second flash due to its long lifetime at this temperature. A very pronounced permanent production of 1,3,5,7-octatetraene was produced in this manner, whereas none of this product was produced when the time interval between flashes was long enough to permit virtually all of the Y to disappear prior to the second flash. This is conclusive evidence that stable octatetraene can be produced by the photolysis of Y. Photolysis of X may also contribute to the biphotonic production of octatetraene, but the lifetime of X is too short to permit an analogous study of this transient with the apparatus used in this investigation.

Discussion

The results definitely establish the formation of two short-lived products in the photolysis of I. These species apparently are not of radical or triplet nature, since the decay is strictly first order at all concentrations and is not influenced by oxygen, and since no important permanent decomposition was observed. Triplets would be expected to be at least partially quenched by second-order triplet–triplet reactions and also to be very sensitive to oxygen, whereas radicals would be expected to give rise to permanent photochem-

ical change by reactions with the solvent. One may therefore assume that the transient species are isomers of the starting compound, I.

The long-lived transient, Y, has a characteristic absorption spectrum which is almost identical with that of stable 1,3,5,7-octatetraene. The synthesis of this latter compound described by Woods and Schwartzman[10] has been shown to produce exclusively the trans,-trans isomer.[12] Recently the cis,trans isomer has been synthesized[11] and found to have an ultraviolet absorption spectrum virtually indistinguishable from that of the trans,trans isomer save for small changes in the λ_{max} extinction coefficients. A synthetic approach that would ordinarily be expected to produce the cis,cis isomer was surprisingly found[11] to yield I instead. Since about 4% of transient Y was produced in a flash that resulted in no more than 1% permanent decomposition of I, it is evident that I is regenerated from Y. These facts clearly lead to the conclusion that Y is cis,cis-1,3,5,7-octatetraene which rapidly recyclizes at room temperature to I. The analogous ring closing of 1,3,5-hexatriene has been studied by Lewis and Steinen.[13] The cis and trans isomers of this molecule, which have nearly identical ultraviolet spectra, are both stable at room temperature. At elevated temperatures the cis isomer cyclizes to 1,3-cyclohexadiene by means of a first-order process. An extrapolation of the published data[13] indicates that cis-1,3,5-hexatriene would have a lifetime of a few seconds at about 200°, comparable to that observed for cis,cis-1,3,5,7-octatetraene at 25°. The greater stability of the hexatriene isomer is found to result from the higher (29 kcal/mole) activation energy for cyclization[13] as compared to the value (17 kcal/mole) observed for octatetraene in the present work. The lower barrier for closing the eight-membered ring can be easily rationalized if one considers the steric problem of rotating the conjugated triene and tetraene into a configuration such that the p orbitals on the end carbon atoms can overlap and begin to form a σ bond as the transition state is approached. Hexatrienes have been shown to cyclize thermally by a disrotatory process.[14] If a Dreiding model of cis-1,3,5-hexatriene is rotated about its single C–C bonds in a disrotatory manner it is observed that considerable "strain" would be required to bring the end atoms into position for appreciable p-orbital overlap. On the other hand, cis,cis-1,3,5,7-octatetraene can be rotated in either the conrotatory (as Woodward and Hoffmann's rules dictate[14]) or the disrotatory manner into configurations that would allow p-orbital overlap at about the normal C–C single bond distance with little or no strain or steric interference. The greater stability of the six- as compared to the eight-membered ring has, of course, no bearing on the kinetics of the cyclization processes.

The flash study showed that Y is formed predominantly from the short-lived component X. This compound was seen to have an absorption spectrum very similar to that of the initial compound, I, except for a shift to longer wavelengths. The strong, long wavelength absorption eliminates isomers without conjugated double bonds. The only isomer of I that has con-

jugated double bonds and might conceivably open rapidly to give 1,3,5,7-octatetraene is known to be a stable thermal isomer of I. The only possibility that comprises all the required characteristics seems to be that X is an unstable cyclic stereoisomer of I. Stable I is the cis,cis,cis isomer which has a "tub" configuration (IV). Although this is the only reasonably strain-free

IV   V

configuration it is likely that other local minima in the potential surface for this system exist at configurations such as the trans,cis,trans "chair" isomer (V), the cis,cis, trans isomer, or the cis,trans,cis isomer, all of which would require only moderate twisting about the double bonds. If one of these isomers results from an electronically excited state of I, the conversion to IV in the ground state may involve a sufficiently high potential barrier to cause the observed ring opening to be the preferred process. The spectrum of one of the stable stereoismers of I would probably be similar to that of IV with a shift to longer wavelengths reflecting the elevated position of its potential energy minimum. The recently reported[15] photosensitized conversion of cis,cis- to cis,trans-1,3-cyclooctadiene lends further support to the proposed identification of X as a photochemically produced stereoisomer of IV.

The stable product of the biphotonic process occurring at high light intensities is undoubtedly one of the stable stereoisomers of 1,3,5,7-octatetraene resulting from photolysis of the unstable cis,cis molecule. Whether it is the cis,trans isomer, the trans,trans isomer, or both, has not been ascertained.

A comparison of the results of this investigation with those reported for previous photochemical studies of I[4–6] reveals an apparent discrepancy in that none of the products appearing in the flash photolysis is observed in the low-intensity studies, and vice versa. In the previous studies only the stable photoproducts were analyzed, and the transient compounds X and Y would obviously not be observed. At low light intensities one would not expect the photoisomerization of Y to occur to any appreciable extent. The formation of II and III was observed after prolonged low-intensity photolysis of I,[4–6] and the quantum yields for their formation may be very low. These photoproducts do not absorb in a region easily accessible to study by the flash technique. It is possible that the 1% decrease in concentration of I observed in this study on flashing at low intensity is due in fact to formation of these products.

In summary we find that photoexcitation of I results in the following transformations

1,3,5-cyclooctatriene $\xrightarrow{h\nu}$ excited state

↑kT

$\xrightarrow{kT}$

cis,cis-1,3,5,7-octatetraene $\longleftarrow$ unstable stereoisomer of 1,3,5-cyclooctatriene

↓$h\nu$

cis,trans- and/or trans,trans-1,3,5,7-octatetraene
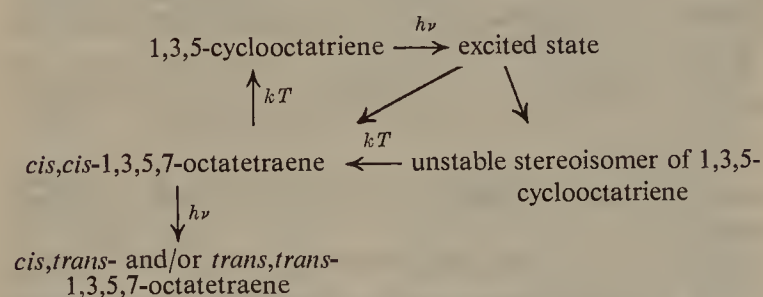
(12) E. R. Lippincott, W. R. Feairheller, and C. F. White, J. Am. Chem. Soc., 81, 1316 (1959).
(13) K. E. Lewis and H. Steinen, J. Chem. Soc., 3080 (1964).
(14) R. B. Woodward and R. Hoffmann, J. Am. Chem. Soc., 87, 395 (1965).

(15) S. H. Liu, ibid., 89, 112 (1967).

A complementary low-temperature matrix isolation study of this system is underway. In addition further studies are planned with the objectives of determining the effect of various substituents on the reaction mechanism and of testing the predictions of Woodward and Hoffmann[14] with respect to the stereospecificity of the thermal and photochemical ring-opening and ring-closing processes.

The One-Electron Oxidation of Triplet Diphenyl-p-phenylenediamine by the Diimine[1]

Henry Linschitz, Michael Ottolenghi, and Rene Bensasson[2]

Contribution from the Department of Chemistry, Brandeis University, Waltham, Massachusetts. Received March 31, 1967

Abstract: The reversible photochemical conversion of N,N'-diphenyl-p-phenylenediamine to its semiquinone positive ion has been studied in acidified EPA, using flash photolysis, over a range of temperatures and concentrations of added diphenyl-p-phenylenediimine. It is shown by direct observation of all three species that the radical ion is formed primarily by reaction of the amine triplet with imine. The kinetics of the reaction suggest the possible intermediate formation of a complex between triplet amine and imine. Rate constants and activation energies are also given for the dismutation reaction of the radical ion. The question of "direct" photoionization of the amine is discussed.

The redox couple N,N'-diphenyl-p-phenylenediamine (DPPD) and the corresponding diimine constitutes a convenient system for the study of reversible photoredox phenomena. The two forms of the couple are readily interconvertible, and the intermediate semiquinone (positive ion) is sufficiently stable so that it may be independently characterized and followed during reaction. In previous work on this system it was demonstrated that the semiquinone ion could be obtained either by reversible photoxidation of the amine or photoreduction of the imine.[3] A kinetic study of this and related systems is now being made, using flash methods. In this paper we describe a new reaction between the triplet state of the diamine and unexcited diimine, leading to the semiquinone ion.

Experimental Section

1. Materials. Eastman DPPD was treated with Norit-A in benzene or ethanol and recrystallized several times from these solvents. The diimine was prepared by chromic acid oxidation of DPPD in glacial acetic acid[4] and recrystallized several times from ethanol and petroleum ether. The product was further purified by chromatography on silica gel, using benzene–ethyl acetate (2:5) as eluent. Isopentane (Phillips or Eastman) was washed with cold concentrated H_2SO_4 and $NaHCO_3$ solutions, stored over Drierite, and distilled from sodium. Ether was purified by distillation either from sodium or $LiAlH_4$. Ethanol was refluxed over CaO and distilled and redistilled from sodium. Acetic acid was Fisher, A.R. grade. EPA solvent was the ether–isopentane–alcohol mixture, in 8:3:5 volume ratio. A slightly acidified EPA, containing 3.5% glacial acetic acid, was much used in this work and is denoted here as EPAG.

For convenience in the following discussion, we use the notation diamine = RH_2, diimine = R, semiquinone positive ion = RH_2^+.

2. Extinction Coefficients of R, RH_2, and RH_2^+. The absorption spectra of R, RH_2, and RH_2^+ are shown in Figure 1. The molar decadic extinction coefficients of R and RH_2 in EPA or ethanol were found at their respective absorption peaks to be $\epsilon^R_{450} = 7.4 \times 10^3$ and $\epsilon^{RH_2}_{307} = 2.40 \times 10^4$. These values agree with previous results of Church[5] to within 2%. The semiquinone positive ion, RH_2^+, was prepared as before, by mixing ethanol or EPA solutions of amine and imine and acidifying with acetic acid.[3] To determine the extinction coefficient of RH_2^+, the reaction was carried out in vacuo, in an ampoule carrying suitable side arms for the spectrophotometer absorption cell and for degassing the three reagent solutions on the vacuum line before mixing.[6] The precision of this method is limited by the presence of oxidizing or reducing impurities in the solutions of R and RH_2, by uncertainties in the extent of conversion (the spectra of R and RH_2^+ overlap at 450 mμ), and by the instability of the radical. The most reproducible data were obtained using very large molar ratios (100 to 200) of RH_2/R, working at high acidities (EPA/acetic acid = 1), and correcting for radical formation in blanks containing no imine. In 50% acetic acid–EPA, at these high amine–imine ratios, the reaction is essentially complete.[3] The molar decadic extinction coefficient found for RH_2^+ at 710 mμ is $\epsilon^{RH_2^+}_{710} = 1.10 \times 10^4$, with an estimated accuracy of ±10%. This is somewhat smaller than the value 1.37×10^4 given earlier.[3]

Since our flash work was carried out in EPA containing 3% acetic acid (EPAG) instead of the 50% solution used for the extinction coefficient calibration, attempts were made to obtain $\epsilon(RH_2^+)$ in more dilute acid media. However, even with 25% acid, conversion to the radical ion was quite incomplete and the intended extrapolation of $\epsilon(RH_2^+)$ to the 3.5% mixture could not be achieved. Nevertheless, the band shapes and relative peak heights of the RH_2^+ spectrum, obtained photochemically (see below), were essentially the same in EPAG as in 50% acetic acid–EPA and did not change detectably with temperature. The semiquinone extinction coefficients were therefore taken to be independent of medium and temperature variation, over the range used here. Table I summarizes the values of the extinction coefficients of DPPD, the diimine, and radical ion at convenient wavelengths.

3. Preparation of Samples and Flash Technique. Test solutions were degassed on the vacuum line by freeze–thaw cycles with vigorous agitation[7] and were sealed off under "sticking vacuum" in an

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(2) NATO Fellow, 1964–1965 (from Laboratoire de Chimie Physique, Faculté des Sciences, Paris).

(3) H. Linschitz, J. Rennert, and T. M. Korn, J. Am. Chem. Soc., 76, 5839 (1954).

(4) J. Picard, Ber., 46, 1853 (1913).

(5) S. E. Church, Ph.D. Thesis, Syracuse University, 1957.

(6) We wish to thank Mr. Wilmon Willen-Bryan for assistance with these experiments.

(7) H. Linschitz, C. Steel, and J. A. Bell, J. Phys. Chem., 66, 2574 (1962).
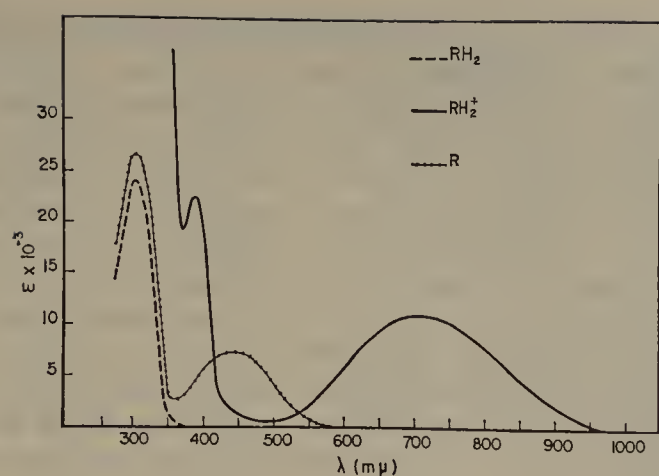
Figure 1. Absorption spectra: diphenyl-*p*-phenylenediamine in ethanol (dashed line); diphenyl-*p*-phenylenediimine in ethanol (dotted line); semiquinone positive ion in 50% EPA–acetic acid (solid line).

ampoule assembly carrying a 5-cm flash irradiation cell (quartz) and a 1-cm cell for absorption spectra measurements (Cary Model 14). The flash apparatus and procedure were essentially those previously described,[7,8] except that the four lamps were made of quartz capillary (5-mm i.d., 5.5 cm between electrodes), terminated with quartz standard-taper joints, and filled with oxygen[9] at about

Table I. Molar Decadic Extinction Coefficients

Substance	λ, mμ	$\epsilon \times 10^{-4}$
DPPD (RH$_2$)	307	2.40
Diimine (R)	450	0.74
	390	0.46
DPPD$^+$ (RH$_2^+$)	390	2.20
	450	0.12
	600	0.65
	710	1.10
	750	1.00

10 mm pressure. The electrodes were tungsten or stainless steel, mounted in tapered stainless steel plugs, which were waxed into the ground joints. The lamps were mounted accurately at the outer foci of a four-leaved elliptical reflector.[8] The photolysis cell was placed axially at the central focus in a flat-bottomed un-silvered quartz dewar, through which was passed a controlled flow of cold nitrogen, obtained from a heating coil immersed in liquid nitrogen. Temperatures were measured by a thermocouple placed in the dewar close to the photolysis cell and could be held constant to better than ±0.3° over the available range, from room temperature down to −160°. A square holder, mounted around the dewar, permitted light filters to be interposed between the flash lamps and the photolysis cell. Corning 9863 filters were generally used, which greatly diminished scattered light corrections from the flash in the 400–700-mμ region. The monochromator was a Bausch & Lomb 500-mm grating instrument, and the measuring light source was a battery-operated strip filament tungsten lamp.

4. Phosphorescence Measurements. The flash apparatus was converted to measurement of phosphorescence decay simply by closing the measuring lamp shutter and opening the monochromator slits to 5 mm. Even at our working sample-to-monochromator distance of about 100 cm, enough phosphorescence intensity was available at the photocell to provide good decay curves, at sample temperatures (DPPD) below −140° (see Figure 2G below). Use of the identical sample and experimental configuration to measure both transient absorption and emission permits particularly convenient and accurate kinetic comparisons to be made. In absorption measurements, the slits were always so narrow (1 mm) that sample luminescence introduced negligible errors.

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(8) H. Linschitz and K. Sarkanen, *J. Am. Chem. Soc.*, **80**, 4826 (1958).
(9) S. Claesson and L. Lindqvist, *Arkiv Kemi*, **11**, 535 (1957).

Amine = 4 × 10^{-5} M
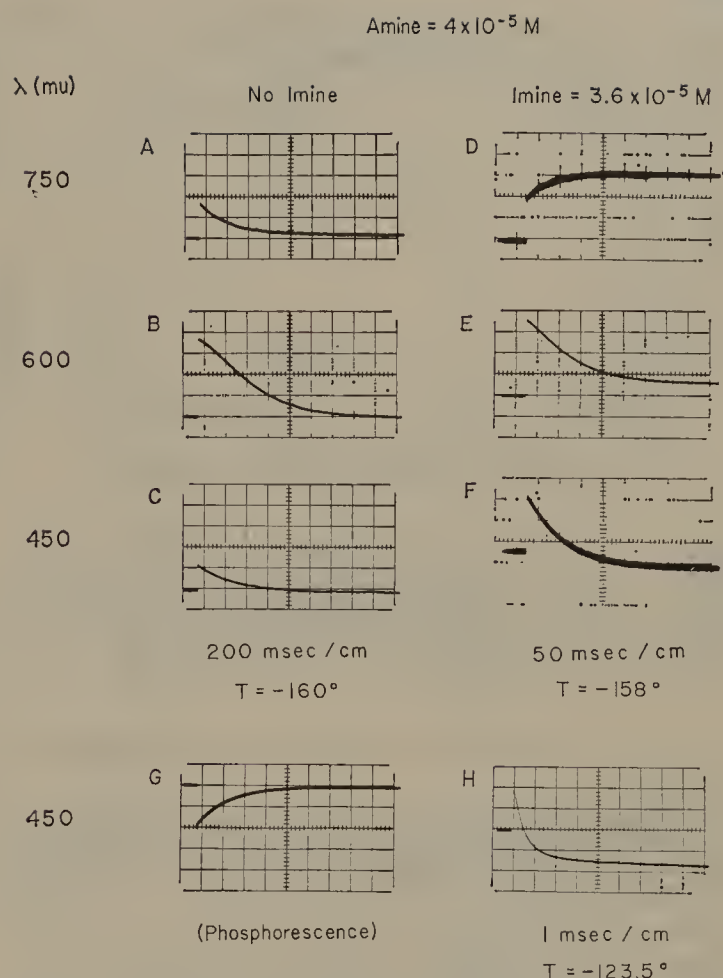
Figure 2. Typical flash oscillograms of solutions of DPPD in EPAG (4 × 10^{-5} M) containing no added imine (A–C, G) and with 3.6 × 10^{-5} M added imine (D–F, H); absorption changes at 750 (A, D), 600 (B, E), and 450 mμ (C, F, H); phosphorescence at 450 mμ (G); A–C, G: −160°, sweep = 200 msec/cm; D–F: −158°, sweep = 50 msec/cm; H: −123.5°, sweep = 1 msec/cm; gain = 1 v/cm except for H, which is 2 v/cm; V_0 (A, D, F, H) = 6 v; V_0 (B, C, E) = 4 v; cell length = 5 cm.

Results

1. General Behavior of DPPD Solutions. Formation of Triplets and Radical Ions. Aerated solutions of the amine in EPA are rather unstable, developing the yellow color of the imine (450-mμ band) after standing for a few hours. Degassed solutions are stable in the dark but are slowly oxidized to the imine upon exposure to ultraviolet light. Addition of small amounts of acid to the EPA prevents this irreversible photoxidation. For example, a 4 × 10^{-5} M solution of DPPD in EPA is about 10% converted to imine under our experimental conditions after 40 (~200 joules) flashes, while a similar solution in the acidified solvent, EPAG, shows no measurable imine formation (<1% conversion) after 60 flashes. To avoid accumulation of imine and ensuing complications (see below), flash studies on "pure" DPPD solutions were therefore made in EPAG.

Figure 2A–C shows some typical oscillograms obtained on flashing such amine solutions at −160°. The immediate result of flashing is an increase in absorption throughout the visible, with a transient peak at 610 mμ. Most of this absorption disappears rapidly, leaving a trace of long-lived intermediate (Figure 2A), which then decays much more slowly, back to the original base line. Figure 3 shows typical difference spectra (referred to the original solution) of a DPPD solution, immediately after flashing (A) and at the completion of the fast decay process (B). It is evident that

TRANSIENT SPECTRA AFTER FLASHING
"PURE" DPPD

□ t = 50 μsec (triplet)
○ t = 40 msec (radical-ion)
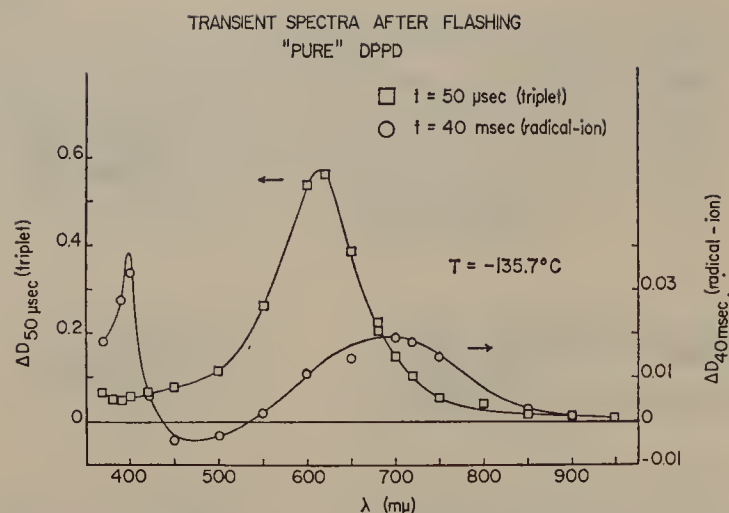
T = -135.7°C

Figure 3. Spectral changes following flash excitation of "pure" DPPD (4×10^{-5} M) in EPAG: □, 50 μsec after flash (left-hand scale); ○, 40 msec after flash (right-hand scale); $-135.7°$; cell length, 5 cm. Note lack of 390-mμ peak in initial flash spectrum and slight bleaching at 450 mμ in long-lived transient.

the two decay periods correspond to two different intermediates.

At temperatures below $-140°$, DPPD solutions in EPAG emit a blue phosphorescence (maximum near 450 mμ), detectable in the flash apparatus. The decay of this phosphorescence corresponds precisely to the decay of the transient absorption peak at 610 mμ (Figure 2G and 2A–C) at all temperatures studied (Figure 5, below). We therefore assign the main short-lived 610-mμ transient to the triplet state of DPPD.

The second (long-lived) transient, which appears in very much smaller amount, has absorption maxima at 390 and 710 mμ, with peak heights in the ratio 2:1. Comparison of Figure 3B with Figure 1C shows the close similarity of the transient spectrum to that of RH_2^+, as prepared by either chemical or photochemical oxidation of RH_2,[3] and immediately identifies the long-lived intermediate as the semiquinone positive ion.

2. Flash Photolysis of Pure Imine Solutions. At room temperature, flashing degassed solutions of imine in EPAG causes an immediate drop at the 450-mμ band and a stoichiometrically equivalent (1:1) rise at the radical-ion peaks at 390 and 710 mμ. The semiquinone fades by second-order kinetics, but no imine regeneration is observed. The first product of the irreversible photobleaching reaction, or at least a major product, is the amine. This is indicated by the gradual appearance, after a few flashes, of the amine triplet band at 610 mμ, as well as increased yields of RH_2^+ (see below). Moreover, the irreversible absorption drop at 450 mμ is not accompanied by a corresponding decrease at the 307-mμ imine band, suggesting that the development of the overlapping amine band compensates for the disappearance of imine absorption in this region.

As the temperature is lowered, the extent of transient radical formation and equivalent irreversible bleaching of imine in EPAG decrease, so that below $-145°$ no absorbance change on flashing is observed anywhere in the available spectral region. In the absence of acidic solvent components, the yields of irreversible bleaching are extremely small, even at room temperature. Thus, in ether–isopentane, neither transient changes nor irreversible bleaching can be detected in flashed imine solutions in the whole range from room temperature down to $-145°$.

3. Flash Photolysis of Mixed Amine–Imine Solutions at Low Temperature. Flash excitation of mixed amine–imine solutions in EPAG causes some irreversible bleaching of the imine. This bleaching diminishes as the temperature is lowered and becomes negligible below $-110°$. Both the extent of imine bleaching and its temperature dependence are similar to that observed in pure imine solutions, and we attribute this, as before, to direct photoreduction of imine, quite independent of any specific amine participation. In this section, we confine our discussion to phenomena observed in the low-temperature range (below $-120°$) in which complications due to irreversible side reactions play no role.

In mixed amine–imine solutions, flashing produces the same two transients that are observed with "pure" amine, $^3RH_2$ and RH_2^+, but the detailed pattern of the changes is altered. The initial result of flashing is, again, a broad transient absorption, peaking at 610 mμ (Figure 2D–F), and assigned to the triplet. Allowing approximately for inner filter effects due to overlapping amine–imine absorption, the triplet yield is about the same as in solutions containing amine alone. However, the radical-ion band at 390 mμ is now found to develop strongly as the triplet decays. That the enhanced 390-mμ band is indeed due to radical-ion formation is shown by a corresponding rise near 710 mμ, although this is somewhat obscured by the overlapping 610-mμ triplet absorption. However, the far-red growing-in is easily seen at wavelengths beyond 730 mμ, as in Figure 2D. Finally, the absorbance decay at 610 and development at 390 and 750 mμ is accompanied by a bleaching near 450 mμ, the absorption peak of the imine (Figure 2F,H). These data alone do not indicate whether the observed bleaching at 450 mμ, which increases with imine concentration, results from an *initial* bleaching of imine, simultaneous with triplet formation and masked by the overlapping triplet absorption, or is due to imine disappearance *accompanying* the triplet decay. The question is resolved by measurements of the ratio of *initial* absorbance changes at 610 and 450 mμ. The data of Table II show that this ratio, $[\Delta D(610)/\Delta D(450)]_{t=0}$, is 7.0 ± 0.5 in "pure" amine solution and remains constant, independent of the concentration of added imine. Thus, the initial flash difference spectrum is constant, and the bleaching at 450 mμ must result from processes occurring *after* the flash. This conclusion is in agreement with the absence of any observable phototransients in pure imine solutions at low temperatures.

Figure 4 shows typical difference spectra of a mixed amine–imine EPAG solution, immediately after flashing and at a time corresponding to completion of the 610-mμ decay or the 390- or 750-mμ development. Comparison of Figures 1, 3, and 4, together with the remarks above, indicates that we are observing a reaction between amine triplet and imine, to form the semiquinone positive ion

$$^3RH_2 + R + 2H^+ \longrightarrow 2RH_2^+ \qquad (I)$$
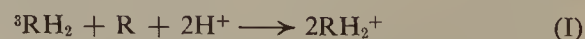
the two protons being contributed by the solvent.[3]

This interpretation is unequivocally established by the kinetics and magnitudes of the observed spectral changes. Table II and Figure 5 show that the (pseudo-first-order, see below) rates of absorbance decay at 600

Table II. Absorbance Changes in Flashed DPPD-Imine Solutions, and Kinetics of Triplet Decay[a]

| Imine × 10⁵, M | Temp, °C | ΔD(³RH₂)[b] | | ΔD(RH₂⁺)[c] | | Rate constant, k', sec⁻¹ | | | | ΔD₆₀₀/ΔD₄₅₀ |
		600 mμ	450 mμ	390 mμ	600 mμ	600 mμ	450 mμ	390 mμ	Phosphorescence	(t = 0)
<0.1	−135.7	0.537	0.076	0.036	0.009	210	218			7.1
...	−151	1.0	0.133	0.056	0.013	21	27			7.5
...	−159.3	0.854	0.127			2.5	2.8			6.7
...[d,e]	−160	1.15	0.162	0.013[g]	0.005	3.1	3.6	3.6[g]	3.6	7.1
...[d,f]	−133	1.8		0.01	0.007	535				
0.4	−152	0.770			0.022	30				
0.54	−135.5	0.480		0.100	0.027	830	1050			
0.95	−147	0.890	0.130	0.264	0.070	170	205	212		6.8
1.5	−149	0.430		0.178	0.042	110				
1.5	−158	0.377		0.144	0.034	18.4		18.9		
1.9	−156	0.490	0.070	0.229	0.064	33	30	41		7.0
2.56	−111	0.512		0.320	0.094	8000	7600	10,100		
2.8	−155.5					36.7				
2.8	−153.3					65				
2.8	−138.9					1050				
3.6	−158					35.5	34	34.5[g]	34	
5.3	−152	0.210	0.034	0.112	0.029	230		230		6.2
6.3	−153.6	0.270		0.162	0.042	170		170		
6.3	−155	0.280		0.159	0.042	140		160		
6.3	−156.4	0.377		0.222	0.057	96		125		
6.3	−149	0.376			0.065	530				
6.3	−143.2	0.342		0.200	0.059	1540				
6.3	−138.5	0.376			0.065	3450				

[a] Path length, 5 cm; DPPD = 4 × 10⁻⁵ M. [b] Measured at t = 0; variation is due mainly to different flash energies (200–800 joules). [c] Measured at completion of initial fast decay (600 mμ). [d] Freshly distilled EPA. [e] DPPD freshly recrystallized six times from ethanol. [f] DPPD = 7 × 10⁻⁵ M, flash energy = 800 joules. [g] Measured at 750 mμ.

mμ (disappearance of ³RH₂), phosphorescence decay at 450 mμ (³RH₂), bleaching at 450 mμ (disappearance of R), and growing-in at 390 and 750 mμ (formation of RH₂⁺) are all precisely the same, and vary with imine concentration in the same way. The stoichiometric

mined with good precision. However, the values of the concentration ratios, $\Delta[RH_2^+]/\Delta[R]$, will reflect errors in the extinction coefficients as well as variations in the intensity of successive flashes required to obtain the ΔD's at different wavelengths. The data of Table
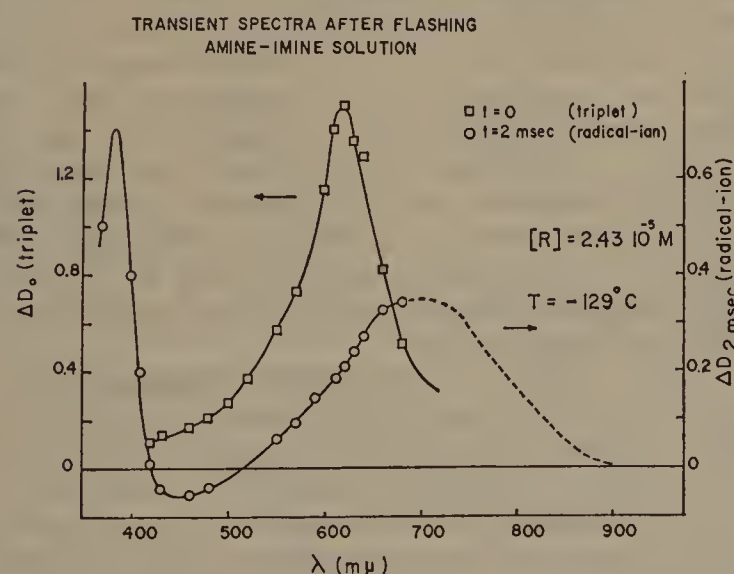
Figure 4. Spectral changes following flash excitation of DPPD (4 × 10⁻⁵ M) with added imine (2.4 × 10⁻⁵ M) in EPAG solution: □, immediately after flash (left-hand scale); ○, 2 msec after flash (right-hand scale); −129°; 5-cm cell.

Figure 5. Kinetics of processes following flashing DPPD (4 × 10⁻⁵ M) in EPAG solution; upper line (A) no added imine, −160°; middle line (B), imine = 3.57 × 10⁻⁵ M, −158°; lower line (C), imine = 5.27 × 10⁻⁵ M, −152.5°. Absorbance decay at 600 (○), 750 (◓), and 450 mμ (●); absorbance development at 750 (△) and 390 mμ (▲); □, phosphorescence at 450 mμ; S_0 = reading immediately after flash; S_t = reading at time t after flash.

ratio of imine bleaching to radical formation—may also be obtained from the flash data, using the extinction coefficients of Table I. In Table III, which summarizes some typical results, the ΔD's refer to absorbance changes measured at the completion of the triplet decay or development of the radical-ion bands. Since the lifetime of the radical is very much longer than that of the triplet at these temperatures (seconds compared with milliseconds), the ΔD's may be experimentally deter-

III thus demonstrate with acceptable accuracy that two radical ions are formed per imine reacted, in accord with reaction I.

The possibility that excited imine is involved in the oxidation of ³RH₂ may be ruled out for two reasons. First, the lack of any visible absorbance change on flashing pure imine solutions at low temperatures in-

Table III. Long-Lived Flash Transient Absorbance Changes and Stoichiometry of Amine–Imine Reaction[a]

Temp, °C	Imine, R × 10⁵ M	ΔD₃₉₀	ΔD₆₀₀	ΔD₇₁₀	−ΔD₄₅₀	Δ[RH₂⁺]/Δ[R] at λ[b] 390 mμ	600 mμ	710 mμ
−154	1.89	0.244	0.064		0.032	1.96	1.67	
−129	2.43	0.520	0.155		0.060	2.12	1.99	
−111	2.56	0.320	0.094		0.036	2.15	2.01	
−158	3.65		0.118		0.046		1.98	
−99	3.92			1.18	0.292			1.88
−99	6.75			0.85	0.214			1.86
−105	6.75			1.30	0.260			2.18
−116	6.75			1.40	0.323			1.98
−122	6.75			1.40	0.323			1.98

[a] DPPD concentration = 4×10^{-5} M. [b] To correct for overlapping R and RH₂⁺ absorption at 450 and 390 mμ; this is calculated from the formula $\Delta D_\lambda/\Delta D_{450} = [x\epsilon(\text{RH}_2^+)_\lambda - \epsilon(\text{R})_\lambda]/[x\epsilon(\text{RH}_2^+)_{450} - \epsilon(\text{R})_{450}]$, where $x = \Delta[\text{RH}_2^+]/\Delta[\text{R}]$ and the ϵ's are given in Table I (note: ΔD_{450} is negative).

dicates that the deactivation of excited imine is very rapid, compared to the time required for radical-ion formation. Second, the data of Figure 5 and Table III refer to observations on the 450-mμ absorption band of *ground*-state imine, whose reaction is thus directly observed.
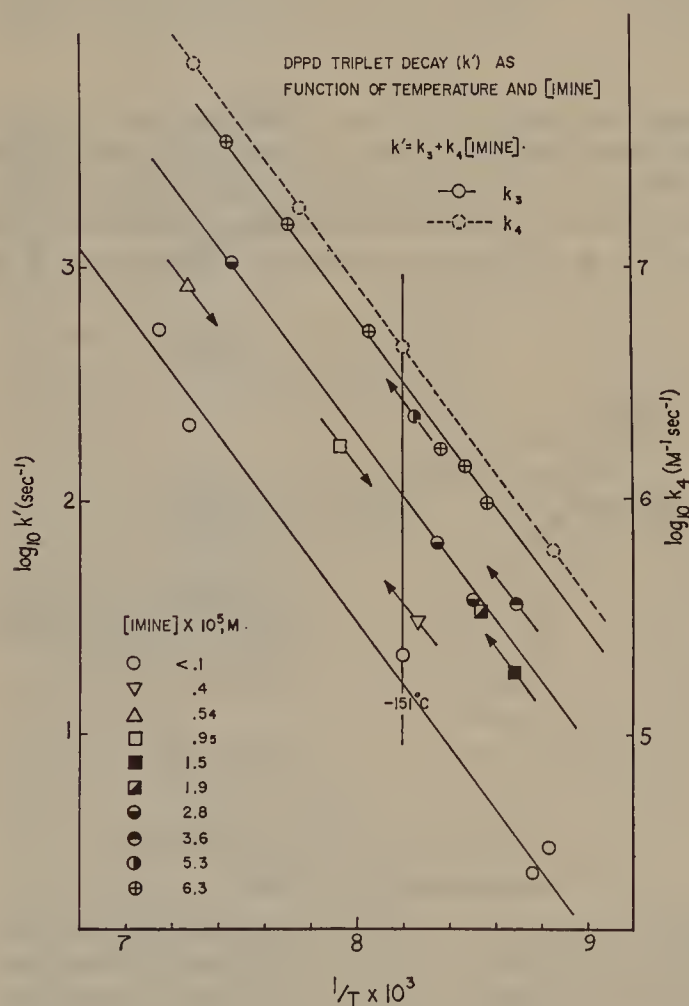
Figure 6. DPPD triplet decay (measured at 600 mμ) as a function of temperature and imine concentration: solid lines, log k' (left-hand scale); dotted line, log k_4 (right-hand scale); [R] as indicated.

4. Kinetics and Evaluation of Rate Constants for Triplet Amine–Imine Reaction.

We write the following sequence, representing the steps in the photochemical amine–imine reaction at low temperature (−100 to 160°) in weakly acidic media

$$\text{RH}_2 \underset{k_1}{\overset{h\nu}{\rightleftarrows}} {}^1\text{RH}_2^* \tag{1}$$

$$ {}^1\text{RH}_2^* \xrightarrow{k_2} {}^3\text{RH}_2^* \tag{2}$$

$$ {}^3\text{RH}_2 \xrightarrow{k_3} \text{RH}_2 \tag{3}$$

$$2\text{H}^+ + {}^3\text{RH}_2 + \text{R} \xrightarrow{k_4} 2\text{RH}_2^+ \tag{4}$$

$$2\text{RH}_2^+ \xrightarrow{k_5} \text{R} + \text{RH}_2 + 2\text{H}^+ \tag{5}$$

$$2\text{RH}_2^+ \xrightarrow{k_6} \text{products} \tag{6}$$
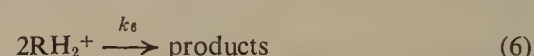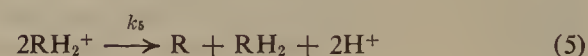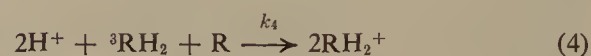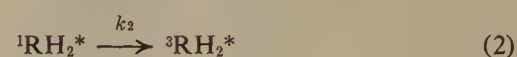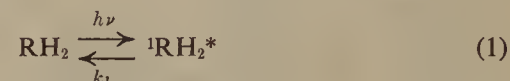
The triplet–imine redox reaction (k_4) is slow compared to the competing triplet decay (k_3), and relatively high concentrations of imine must be used to obtain good conversion of ${}^3\text{RH}_2$ to RH_2^+. The fractional conversion of imine to radical ion is correspondingly small. For example, the data of Table II show that at the flash energies and DPPD concentrations used here, and at imine concentrations of 1×10^{-5} M, only about 15% of the imine reacts to form the semiquinone ion. At higher imine concentrations, the fraction converted is even less. Under these circumstances, the decay of ${}^3\text{RH}_2$ and formation of RH_2^+ becomes pseudo first order, as shown in Figure 5, with an effective rate constant $k' = k_3 + k_4[\text{R}]$. The constant, k_4, is most simply and directly determined from the variation of k' with imine concentration.

A large number of experiments are summarized in Figure 6, which plots log k' (Figure 5) *vs.* T^{-1} for various imine concentrations. Figure 6 shows that within experimental error the temperature coefficient of k' is independent of imine concentration over the entire range of triplet decay, from practically complete transition to the amine ground state to almost complete scavenging by the imine and conversion to the radical ion. This striking result requires that k_3 and k_4 have the same activation energy, which is found from Figure 6 to be 6200 ± 200 cal/mole. Since it is experimentally very inconvenient, with our cooling technique, to adjust the temperature precisely to a given setting for a large number of determinations, these results were used to correct the experimental k' values at measured temperatures to nearby standard temperatures, at which the effect of varying the imine concentration could then be isolated. The resulting plots of k' (corrected) *vs.* [R] are reasonably linear, as indicated by Figure 7, which gives a value of $k_4 = 4.5 \times 10^6$ M^{-1} sec⁻¹ at −151°. From the slopes of such lines we obtain the values of
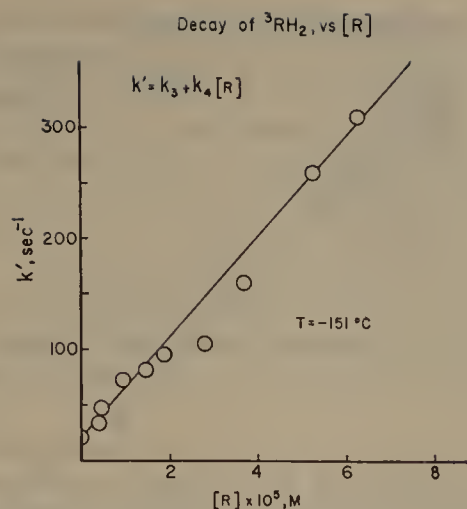
Figure 7. Effective first-order rate constant, k', as function of imine concentration, $[R]$; data from Figure 6, corrected to $-151°$.

Figure 8. (Radical–ion/triplet amine) ratio, as function of imine concentration: $\bigcirc$, $[\Delta D(390, \text{ long-lived})/\Delta D(600, t = 0)]$, left-hand scale; $\square$, $[\Delta D(600, \text{ long-lived})/\Delta D(600, t = 0)]$, right-hand scale; points at all temperatures (-110 to $-160°$).

k_4 shown by the upper (dotted) line of Figure 6 (right-hand scale). In the interval from -100 to $-160°$, k_3 and k_4 are given by

$$k_3 = 1.35 \times 10^{12} \exp(-6200/RT) \text{ sec}^{-1}$$

$$k_4 = 4.5 \times 10^{17} \exp(-6200/RT) \ M^{-1} \text{ sec}^{-1}$$

In addition to the kinetic determinations of the rate constants k_3 and k_4, as summarized in Figures 6 and 7, the ratio k_3/k_4 and the triplet extinction coefficient may be obtained from measurements of the relative triplet and semiquinone yields, as function of imine concentration. According to the above reaction scheme, the quantum yield of semiquinone, $\varphi(RH_2^+)$ is

$$\varphi(RH_2^+) = 2\varphi(^3RH_2)\left(\frac{k_4[^3RH_2][R]}{k_3[^3RH_2] + k_4[^3RH_2][R]}\right) \quad (7)$$

or

$$\frac{\varphi(^3RH_2)}{\varphi(RH_2^+)} = \frac{1}{2}\left(1 + \frac{k_3}{k_4[R]}\right) \quad (8)$$

Since the triplet and semiquinone are *both* formed as a result of the *same* light flash, the ratio of φ's is also the ratio of the corresponding chemical yields. At wavelengths where only the imine has overlapping absorption, eq 8 may then be written, in terms of the directly observed absorbance changes, as

$$\frac{\Delta D_{\lambda(t=0)}}{\Delta D_{\lambda'(\max)}} = \frac{\epsilon(^3RH_2)_\lambda}{[2\epsilon(RH_2^+) - \epsilon(R)]_{\lambda'}}\left(1 + \frac{k_3}{k_4[R]}\right) \quad (9)$$

in which $\Delta D_{t=0}$ is measured immediately after the flash and $\Delta D_{\max}$ is the long-lived absorption at the completion of triplet decay.

In Figure 8, we plot the absorbance ratios against imine concentration, using measurements at 600 mμ for both $\Delta D_{t=0}$ and $\Delta D_{\max}$ and 390 mμ for $\Delta D_{\max}$ (Table II). Data at all temperatures are included, since k_3/k_4 has been shown to be temperature independent. The limiting value of the absorbance ratio with increasing $[R]$ corresponds to complete trapping and conversion of $^3RH_2$ to RH_2^+. From this limiting ratio (~ 0.60) and the data of Table I, we obtain for the molar decadic extinction coefficient of the amine triplet at 600 mμ the value $\epsilon = (6.7 \pm 1.5) \times 10^4$.

The application of eq 9 to our results is shown in Figure 9. The solid line in Figure 9 is calculated from the kinetic measurements at $-151°$ (Figures 6 and 7),
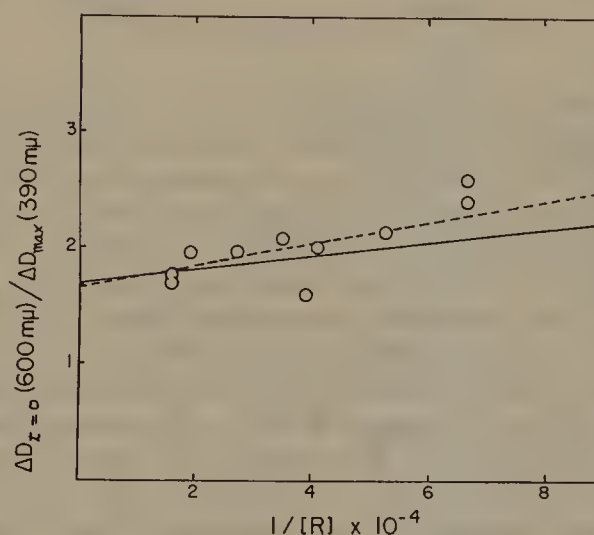
Figure 9. $[\Delta D(600 \text{ m}\mu, t = 0)/\Delta D(390 \text{ m}\mu, \text{ long-lived})]$ vs. $[R]^{-1} \times 10^{-4}$; data of Figure 8: solid line, calculated from eq 9, using k_3 and k_4 from rate measurements (Figures 5–7) and extinction coefficients from Table I and Figure 8; dotted line, from yield data.

taking $k_3 = 16.5 \text{ sec}^{-1}$, $k_4 = 4.5 \times 10^6 \ M^{-1} \text{ sec}^{-1}$, and $\epsilon_{600}(^3RH_2) = 6.7 \times 10^4$, while the dotted line is drawn to fit the yield data. The agreement is certainly within the experimental spread, for the points at high imine concentration. At very low $[R]$, there appears to be a tendency for the experimental points to deviate upward from the calculated line.

5. Kinetics of Semiquinone Decay. The final process observed following flashing of DPPD–imine solutions is the decay of the long-lived transient bands at 390 and 710 mμ and, at a corresponding rate, recovery of absorption at 450 mμ. Since the degree of irreversibility per flash is small, and the ratio of imine reacted to radical ion formed has been shown to be 1:2 (Table III), the final recovery process must be the dismutative back-reaction (step 5, above)

$$2RH_2^+ \xrightarrow{k_5} R + RH_2 + 2H^+$$

Direct confirmatory measurements of the extent of recovery of amine are difficult, because of the overlapping R, RH_2, and RH_2^+ spectra.

The kinetics of the recovery process are second order, as shown by linear plots of $(\Delta D_\lambda)^{-1}$ vs. time, for mea-
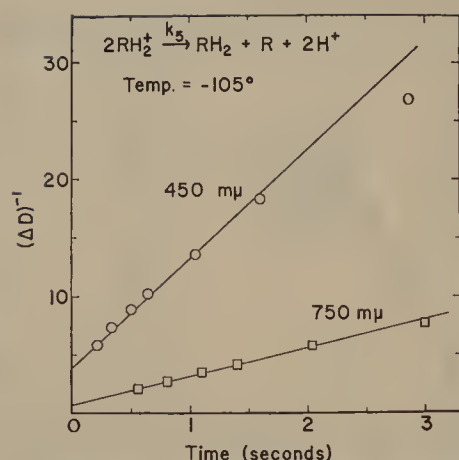
Figure 10. Second-order kinetics (k_5) of radical-ion decay, ΔD^{-1} vs. time: O, 450 mμ; □, 750 mμ; $-105°$.

Figure 11. Ln k_5 vs. $T^{-1} \times 10^3$: O, measured at 710 and 750 mμ; □, measured at 450 mμ. The line favors results which we believe to be most reliable.

surements at both 450 and 710 mμ (Figure 10). Defining the rate constant by

$$-\frac{d[RH_2^+]}{dt} = k_5[RH_2^+]^2 = 2\frac{d[R]}{dt}$$

k_5 is obtained from the slope, m, of the $(\Delta D_{750})^{-1}$ vs. time plot as $k_5 = ml\epsilon_{750}(RH_2^+)$, where l is the cell path length (5 cm). At 450 mμ, again taking account of the stoichiometry and overlapping radical and imine absorption, we have $k_5 = ml[\epsilon(RH_2^+) - \frac{1}{2}\epsilon(R)]_{450}$.

The kinetic results are summarized in Table IV. The recovery rate constants measured at 710 or 750 mμ are in good agreement with those obtained at 450 mμ, particularly in view of the sensitivity of the latter values to errors in the extinction coefficients. In the temperature range -90 to $-135°$, $k_5 = 3.6 \times 10^{10} \exp(-4200/RT)$ M^{-1} sec^{-1} (Figure 11). The rate of radical-ion decay appears to be sensitive to catalytic impurities. In early experiments, using less carefully purified materials, several-fold higher rates were observed, with somewhat higher activation energies as well.

Table IV. Kinetics of Radical-Ion Decay and Imine Recovery

Temp, °C	Imine × 10⁵, M	$k_5 \times 10^{-5}$ M^{-1} sec^{-1}	
		710 mμ	450 mμ
−99	3.9		2.2
−99	6.75	1.80[a]	1.93
−105	6.75	1.21[a]	1.23
−115.5	3.9	0.70	0.75
−116	6.75	0.61	0.81
−121	6.75	0.44	0.64
−123	3.9	0.29	0.28
−130	6.75	0.15	0.15
−131	3.9	0.12	

[a] At 750 mμ.

Discussion

1. Evidence for Complex Mechanism in Triplet Amine–Imine Reaction. While the stoichiometry and formal kinetic scheme of the triplet amine–imine reaction seem to be well established by the results reported here, the experimental bimolecular rate constant, $k_4 = 4.5 \times 10^{17} \exp(-6200/RT)$ M^{-1} sec^{-1}, evidently demands further discussion. Allowing even several times the maximum error in the activation energy of Figure 6, and computing the corresponding smallest possible

value of the preexponential factor of k_4, one still obtains a result which is orders of magnitude greater than any reasonable encounter number. Consideration must also be given to the proton transfers involved in the reaction. Thus, a complex mechanism is indicated.

A simple possibility is the formation of an equilibrated reaction intermediate between $^3RH_2$ and R, which could then decompose to $2RH_2^+$. Protonation might occur either in the formation or decomposition of the complex. Assuming the latter, we have

$$^3RH_2 + R \underset{k_B}{\overset{k_A}{\rightleftharpoons}} (^3RH_2 \cdot R)$$

$$(^3RH_2 \cdot R) \xrightarrow[k_C]{H^+} 2RH_2^+$$
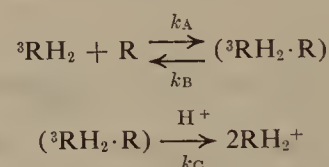
The rate constant k_4 then becomes $k_4 = k_A k_C/k_B$ and $E_4 = E_C + E_A - E_B$. This formulation is attractive since the electron transfer within the complex might be promoted by the very charge-resonance or transfer interactions which contribute to the excimer binding.[10-12] Such charge-transfer complexes have been proposed earlier on the basis of other arguments, in connection with the quenching of excited states,[13,14] and have been conclusively identified by their luminescence.[15,16] It is relevant also to note the possible direct demonstration of excimer formation by recombination of aromatic hydrocarbon cations and anions,[17] a process that is the reverse of the electron transfer *following* excimer formation which is postulated here.

(10) M. T. Vala, I. H. Hillier, S. A. Rice, and J. Jortner, *J. Chem. Phys.*, 44, 23 (1966).
(11) J. N. Murrell and J. Tanaka, *Mol. Phys.*, 7, 363 (1964).
(12) T. Azumi and S. P. McGlynn, *J. Chem. Phys.*, 41, 3131 (1964).
(13) H. Linschitz and L. Pekkarinen, *J. Am. Chem. Soc.*, 82, 2411 (1960).
(14) H. Leonhardt and A. Weller, *Z. Physik. Chem.* (Frankfurt), 29, 277 (1961).
(15) H. Leonhardt and A. Weller, *Ber. Bunsenges. Physik. Chem.*, 67, 791 (1963).
(16) N. Mataga, K. Ezumi, and T. Okada, *Mol. Phys.*, 10, 201, 203 (1966).
(17) E. Chandross, J. W. Longworth, and R. E. Visco, *J. Am. Chem. Soc.*, 87, 3259 (1965).

To account for the pseudo-first-order kinetics (Figures 5 and 7) and the absence of any transient absorption which might correspond to the complex, we need $[^3RH_2 \cdot R] \ll [^3RH_2]$. If we assume this ratio to be less than 10^{-2} for $[R] \sim 10^{-4} M$, then k_A/k_B must be less than $10^2 M^{-1}$. With these limiting values, and taking $k_4 \cong 10^7 M^{-1} \sec^{-1}$ at $-151°$, k_C must then be about $10^5 \sec^{-1}$. Assuming further that k_B/k_C is at least 10 requires that k_A be at least $10^8 M^{-1} \sec^{-1}$. Rough data[18] on the viscosity of EPA in the temperature range of our experiments indicate that this value of k_A is not unreasonable.

Other mechanisms may, of course, be written which do not assume equilibration of the complex. An intuitively satisfying possibility allows the complex either to decompose to the ground state (k_B) or to react with the protonating agent to give the radical ion (k_C). With the assumption that $k_B \gg k_C$, this leads to the same formal relationships as before. The observed, rather remarkable, similarity in the temperature dependence of k_3 and k_4 is in agreement with the sense of this mechanism since the main processes controlling triplet decay in fluid solvents appear to be pseudo-first-order quenching reactions.[7,19] Thus, k_3 and k_4 would be expected to have similar properties. This implies, however, that the entire observed activation energy, 6200 cal/mole, should be ascribed to E_A, or that $E_B = E_C$. Under these conditions, the rate of formation of complex becomes much to slow to account for k_4. In addition, this mechanism limits the maximum yield of radical ion at high imine concentrations to $\varphi_{max}(RH_2^+) = 2\varphi(^3RH)_2 \cdot k_C/(k_C + k_B)$. The triplet extinction coefficient thus may be in error by the indicated rate factor, if appreciable quenching by the imine occurs. Taking $k_B/k_C \sim 10$ leads to a molar extinction coefficient tenfold greater than the already quite high value given above. This must be taken as evidence against a competitive imine quenching reaction, despite the parallelism of the k_3 and k_4 Arrhenius plots. Conversely, an independent determination of the triplet extinction coefficient would help clarify the situation. Further speculation on mechanism does not appear to be fruitful, pending the completion of new experiments on this system, particularly on the effect of varying solvent acidity.

2. Relation of Photochemical Amine–Imine Reaction to Ground-State Equilibrium. Solutions of DPPD and the imine in 3% acetic acid–EPA show no semiquinone absorption bands. Much stronger acid is needed to develop the radical.[3] The photochemical reaction may thus be regarded as resulting from a shift in the redox potential of the amine–imine couple upon excitation. Since the absorption spectrum of the radical ion lies at much lower energies than that of the amine phosphorescence, such a shift is in the expected direction, even if the semiquinone is formed initially in its excited state. For the triplet amine–imine reaction, the question must remain open at this time regarding the excitation state of the immediate products of the presumed excimer decomposition. However, the observed back-reaction (k_5) evidently deals with the same species that occur in the ground-state reaction. Thus, flash measurements of the rate of the back-reaction (k_5) af-

ford the possibility of isolating some of the kinetic factors involved in the *ground*-state equilibrium.

3. Does "Direct" Photoxidation of DPPD Occur? We have noted that in flashed EPAG solutions of DPPD containing no *added* imine, the yield of radical ion is extremely low, relative to the triplet (Table II, Figure 3). In other solvents, such as neutral EPA, EP (8:3), ethanol, or tetrahydrofuran, we observe the same general pattern of triplet and traces of radical-ion formation, although the semiquinone/triplet ratio is even smaller than in EPAG, and becomes rather irreproducible. These effects, at least in part, are certainly caused by varying amounts of imine contamination, arising from irreversible photochemical or dark oxidation of the original DPPD solutions. However, the question now arises whether any part at all of the RH_2^+ formed by flashing DPPD in EPAG arises from an *intrinsic* photoionization of the pure amine, producing some RH_2^+ already at $t = 0$, or whether radical formation is entirely and solely due to oxidation of the triplet by unavoidable traces of imine or other oxidizing impurity. This question is of great importance, in view of the many studies which have been made on the mechanism of photoionization in condensed phase,[20] using test substances which are easily oxidized chemically. The fact that no growing-in of radical ion can be seen in flashed "pure" DPPD solutions does not immediately dispose of the matter, since the small amount of radical absorption is overlapped everywhere by the relatively much larger triplet bands, and any radical development would be completely masked by triplet decay.

Using the results of Figure 8, and taking the curve for *pure* amine solutions to pass through the origin, one can estimate that the amount of imine impurity required to produce a semiquinone absorbance of, say, 0.01 in a 5-cm cell would be practically undetectable by standard spectrophotometric means. More sensitive tests are to look for *residual* bleaching effects at 450 mμ, or traces of a 390-mμ peak in the *initial* difference spectrum of flashed "pure" amine solutions. Slight residual bleachings at 450 mμ were indeed found, corresponding closely to the residual radical-ion formation (Figure 2C) while the difference spectrum immediately after the flash showed no trace of a peak at 390 mμ (Figure 3). These results, together with the steady trend of decreasing semiquinone yield with increasingly painstaking amine and solvent purification, lead us to conclude that direct photoejection of electrons from DPPD (either by one or two-photon processes) does not occur in these flash experiments.

This result is to be contrasted with our earlier observations in rigid solvents.[3] The steady irradiation experiments can, of course, detect processes with very low quantum yields. In addition, the flash and rigid solvent experiments have used different excitation sources and further comparisons require information on the wavelength and intensity dependence of photoionization yield. In any event, there can be no doubt that bimolecular oxidation of triplets by suitable reagents affords a simple pathway to form radical ions at low excitation energies. The possibility of this process must be kept in mind in photoionization studies.

(18) H. Greenspan and E. Fischer, *J. Phys. Chem.*, **69**, 2466 (1965).
(19) R. Livingston and W. R. Ware, *J. Chem. Phys.*, **39**, 2593 (1963).

(20) K. D. Cadogan and A. C. Albrecht, *ibid.*, **43**, 2550 (1965), and references therein.

The Chemical Properties of Chlorodifluoramine[1]

Robert C. Petry[2]

Contribution from the Rohm and Haas Company, Redstone Research Laboratories, Huntsville, Alabama. Received March 20, 1967

Abstract: The thermal and photochemical reactions of chlorodifluoramine and aliphatic olefins produce β-chloro-difluoramines, bis(difluoramines), and dichlorides. A study of the equilibrium between chlorodifluoramine and tetrafluorohydrazine–chlorine is reported. Alkyldifluoramines are formed from aliphatic mercurials and chloro-difluoramine.

During an investigation of the interaction of di-fluoramine and Lewis acids, it was discovered that difluoramine and boron trichloride react to yield a new fluoronitrogen, chlorodifluoramine, $ClNF_2$.[3] Some additional methods of preparation have since appeared.[4-7]

Three reactions of this new material have been investigated in some detail: (1) its photochemical decomposition, (2) its reaction with olefins, and (3) its reaction with mercurials. In addition, some observations have been made on its reactions with nucleophilic reagents.

The Chlorodifluoramine–Tetrafluorohydrazine–Chlorine Equilibrium

The absorption spectrum of chlorodifluoramine (Figure 1) shows it to be ultraviolet active in the near-visible region. The following equilibrium was demonstrated by irradiating both a pure sample of chloro-difluoramine and a mixture of tetrafluorohydrazine and chlorine (1:5 mole ratio). This reaction is endothermic as written, but at elevated temperatures it

$$N_2F_4 + Cl_2 \xrightleftharpoons[\quad]{\text{ultraviolet}} 2NF_2Cl \qquad (1)$$
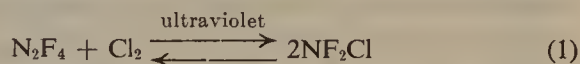
might be a practical route to chlorodifluoramine. Equilibrium constants obtained with four different mixtures of different temperatures are listed in Table I. The experimental procedure involved preparation of a known mixture of two of the three components in a 50-cc Pyrex bulb, thermostating the bulb in a constant-temperature water bath, and irradiating for 10–15 min with a Hanovia EH-4 light source. The lamp was turned off, the bulb removed from the water bath, and the equilibrium mixture expanded into a short path length infrared cell. Duplicate infrared spectra were obtained from which the equilibrium concentrations of $ClNF_2$ and N_2F_4 were determined. No change in the equilibrium concentrations was observed during the sampling period. The sample was then condensed

back into the sample bulb and the procedure repeated at the same or different temperatures. For the first measurements at 49.90°, the mean deviation from the average value of the equilibrium constant was $\pm 5\%$ which was considered adequate in view of the limitations of quantitative infrared analysis. However, as successive measurements at different temperatures were made, the mean deviation increased, indicating deterioration of samples and/or losses due to repeated sampling. Additional data for mixture 4 is presented in Table IV in the Experimental Section.

Table I. Equilibrium Constants for the Reaction $N_2F_4 + Cl_2 \rightleftarrows 2ClNF_2$

Mixture no.	Initial pressure, mm[a]			Temp, °C	K
	N_2F_4	Cl_2	NF_2Cl		
1	55.2	190	...	49.90	0.0057
2	55.2	116	...		0.0054
3	55.2	520	...		0.0052
4	...	406	100		0.0050
1				69.70	0.0161
2					0.0158
3					0.0128
4					0.0130
1				83.10	0.0343
2					0.0374
3					0.0234
4					0.0275
1				41.25	0.0028
2					0.0040
3					0.0024
4					0.0031

[a] The same mixtures were used for all experiments. Experiments were made over a 2-week period in the order shown.

A plot of log K vs. $1/T$ for mixture 4 is shown in Figure 2. The triangles represent the average value of K for the four different mixtures in Table I. The temperature dependence of the equilibrium constant as determined from the data is

$$\log K = -(2640/T) + 5.77$$

giving a $\Delta H = \sim 12$ kcal for reaction 1. Sufficient accuracy was not obtained in these measurements to justify correction of the data for the N_2F_4 dissociation. Recalculation of the equilibrium constant at 83.10° (Table I) by correcting the equilibrium N_2F_4 pressure by the amount dissociated into NF_2 radicals gave a value of 0.0310. The corresponding correction at 29° was negligible.[8]

(2) Deceased. Correspondence regarding this article should be sent to Dr. T. E. Stevens of these laboratories.
(3) Preliminary accounts of the physical and chemical properties of $ClNF_2$ have appeared: R. C. Petry, *J. Am. Chem. Soc.*, **82**, 2400 (1960); R. C. Petry, Abstracts, 138th National Meeting of the American Chemical Society, New York, N. Y., Sept 1960, p 22M.
(4) D. M. Gardner, W. W. Knipe, and C. J. Mackley, *Inorg. Chem.*, **2**, 413 (1963).
(5) T. A. Austin and R. W. Mason, *ibid.*, **2**, 646 (1963).
(6) E. A. Lawton and J. Q. Weber, *J. Am. Chem. Soc.*, **85**, 3595 (1963).
(7) W. C. Firth, Jr., *Inorg. Chem.*, **4**, 254 (1965).

(8) The effect of change in light intensity and wavelength distribu-
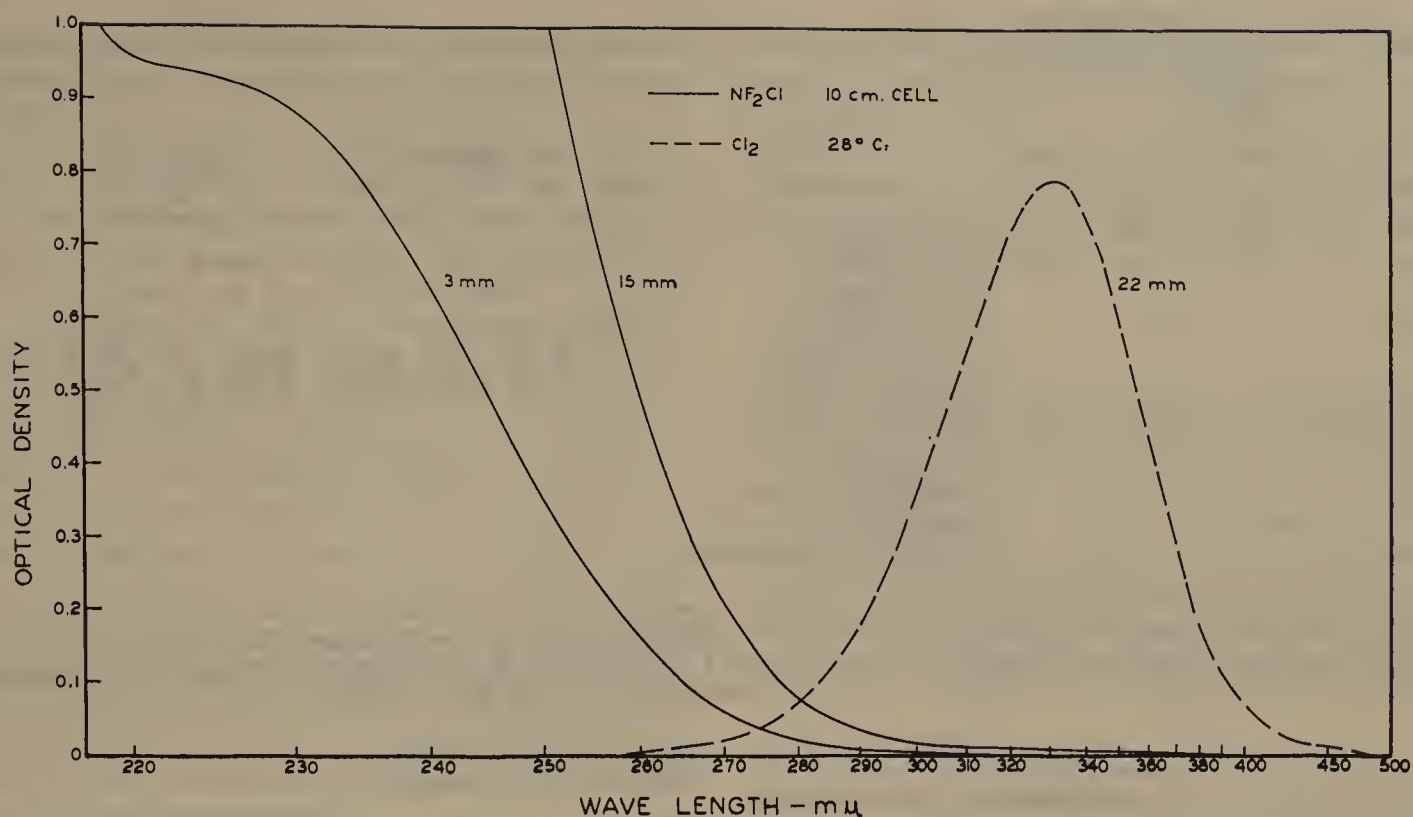
Figure 1. Ultraviolet absorption spectrum of chlorodifluoramine.
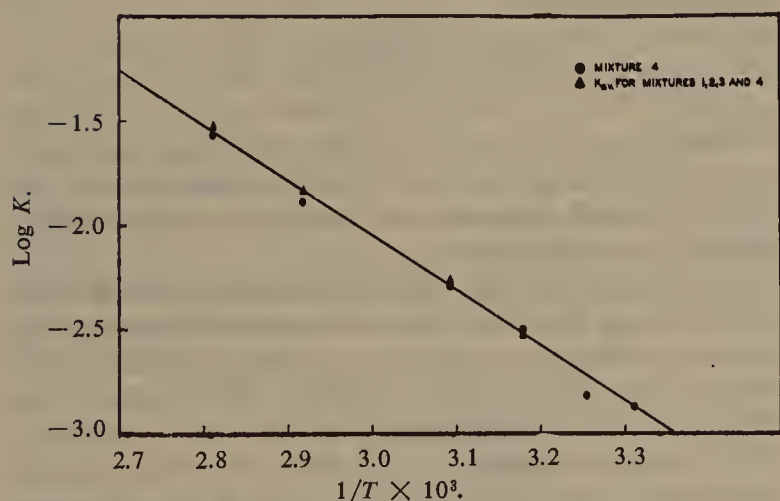
Figure 2. Log K as a function of $1/T$ for the equilibrium $N_2F_4 + Cl_2 \rightleftarrows 2ClNF_2$.

Figure 3. Photochemical decomposition of $ClNF_2$.

From the heat of formation of N_2F_4 $(-2\ \text{kcal})$[9] and the assumption that the temperature dependence of the photochemical equilibrium is a valid measure of ΔH for reaction 1, a heat of formation of approximately 5 kcal was obtained for $ClNF_2$.

The rate of photochemical decomposition of $ClNF_2$ was examined briefly (Figure 3). Chlorodifluoramine at 36 mm pressure in a Pyrex infrared cell (NaCl windows) was irradiated with a Hanovia EH-4 lamp at 27° for 70 min. Both the disappearance of NF_2Cl and the formation of N_2F_4 were followed by quantitative infrared analysis. The decomposition proceeded smoothly and exhibited marked autocatalysis. The decomposition curve with 7% added chlorine is also shown. The catalytic effect of chlorine is clearly demonstrated. The proposed mechanism is given in

tion on the equilibrium have not been studied and it is possible that the observed equilibrium constants may represent a photochemical steady state and not true equilibrium constants for the system.

(9) G. T. Armstrong, S. Marantz, and C. F. Coyle, National Bureau of Standards Report No. 6584, U. S. Government Printing Office, Washington, D. C., 1959.

eq 2–5. The fact that $ClNF_2$ does not decompose in

$$NF_2Cl \underset{\rightleftharpoons}{\overset{h\nu}{}} \cdot NF_2 + \cdot Cl \qquad (2)$$

$$\cdot Cl + NF_2Cl \longrightarrow Cl_2 + \cdot NF_2 \qquad (3)$$

$$Cl_2 \underset{\rightleftharpoons}{\overset{h\nu}{}} 2 \cdot Cl \qquad (4)$$

$$2 \cdot NF_2 \rightleftharpoons N_2F_4 \qquad (5)$$
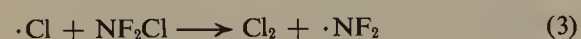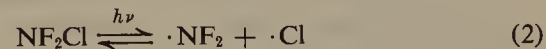
the presence of N_2F_4 (and hence NF_2 radicals) at ambient temperature in the absence of ultraviolet activation indicates that reaction 6 is not involved.

$$\cdot NF_2 + NF_2Cl \longrightarrow N_2F_4 + \cdot Cl \qquad (6)$$
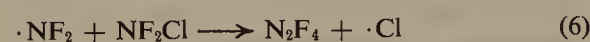
Reaction of Chlorodifluoramine with Olefins

Chlorodifluoramine reacted with aliphatic olefins at elevated temperature (70–130°) to produce a mixture of the bis(difluoramine), the dichloride, and the β-chlorodifluoramine. The results are summarized in Table II.

Table II. Reaction of Chlorodifluoramine and Olefins

Olefin	Reaction conditions Initial pressure, mm	Temp, °C	Time, hr	Products	Yield[a]	Calcd, % C	H	N	Found, % C	H	N	F[19] resonance
Ethylene	100	70	4	ClCH₂CH₂Cl	17							
Ethylene	400	130	12	ClCH₂CH₂NF₂ NF₂CH₂CH₂NF₂[c,f]	91[b]	20.79	3.49	12.13	21.77	3.75	12.91	−52.8φ
Propylene	407	130	6	CH₃CHClCH₂Cl CH₃CHClCH₂NF₂ CH₃CH(NF₂)CH₂Cl CH₃CH(NF₂)CH₂NF[c]	96[d]	27.81 27.81	4.67 4.67	10.81 10.81	27.42 27.86	4.64 4.74	10.62 11.25	−54.4φ −38.6φ
trans-Butene-2[e]	500	120	7	CH₃CHClCHClCH₃ (*dl* and *meso*) CH₃CH(NF₂)CHClCH₃ (*erythro* and *threo*) CH₃CH(NF₂)CH(NF₂)CH₃ (*dl* and *meso*)	95							

[a] Combined adduct yield based on recovered ClNF₂ and olefin. [b] By glpc analysis, the ratio of products was 1.3:2.5:1.0, respectively. [c] Reference 12. [d] By glpc analysis, the ratio of product was 1.2:0.4:1.1:1.0, respectively. [e] Because of the complexity of this mixture, no complete resolution of the mixtures was attained. [f] This product was not obtained in the 70° reaction.

$$NF_2Cl + CH_2{=}CH_2 \longrightarrow ClCH_2CH_2Cl +$$
$$ClCH_2CH_2NF_2 + NF_2CH_2CH_2NF$$

Under the influence of ultraviolet light at room temperature, the reaction took a different course entirely. The photochemical reaction of ethylene with ClNF₂ at ambient temperatures proceeds according to the stoichiometry

$$2NF_2Cl + H_2C{=}CH_2 \longrightarrow ClCH_2CH_2Cl + N_2F_4$$
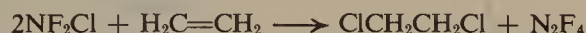
No C–NF₂ products are observed, and relatively long irradiation periods resulted in low conversion to products without decomposition of the unreacted ClNF₂. A plausible mechanism for this reaction is shown in eq 7–10. Since reaction 11 has an activa-

$$NF_2Cl \underset{}{\overset{h\nu}{\rightleftharpoons}} \cdot NF_2 + \cdot Cl \qquad (7)$$
$$\cdot Cl + CH_2{=}CH_2 \longrightarrow ClCH_2CH_2\cdot \qquad (8)$$
$$ClCH_2CH_2\cdot + ClNF_2 \longrightarrow ClCH_2CH_2Cl + \cdot NF_2 \qquad (9)$$
$$2\cdot NF_2 \rightleftharpoons N_2F_4 \qquad (10)$$
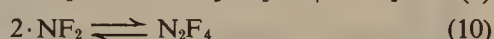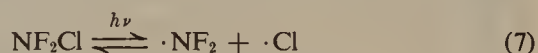
tion energy of about 14 kcal,[10] it would not be expected

$$\cdot NF_2 + CH_2{=}CH_2 \longrightarrow F_2NCH_2{-}CH_2\cdot \qquad (11)$$

to occur in the system under consideration. Reactions 12 and 13 would also lead to C–NF₂ products. No

$$ClCH_2CH_2\cdot + \cdot NF_2 \longrightarrow ClCH_2CH_2NF_2 \qquad (12)$$
$$ClCH_2CH_2\cdot + N_2F_4 \longrightarrow ClCH_2CH_2NF_2 + \cdot NF_2 \qquad (13)$$

estimate is available concerning the activation energy for reaction 13 while that for (12) can be assumed to be very small. The value of K_p for the N₂F₄ dissociation and the experimental conditions employed in the photochlorination experiment with ethylene and ClNF₂ allow an estimation of the mean values of the ratios [·NF₂]/[NF₂Cl] and [N₂F₄]/[NF₂Cl] during the reaction. With the assumption that C–NF₂ products would be detectable at the 5% level in the product fraction, the following equations can be set up.

$$\frac{k_9[ClCH_2CH_2\cdot][NF_2Cl]}{k_{12}[ClCH_2CH_2\cdot][\cdot NF_2]} \geq 20$$

$$\frac{A_1 e^{-E_9/RT}}{A_2 e^{-E_{12}/RT}} \frac{[NF_2Cl]}{[\cdot NF_2]} \geq 20$$

(10) A. J. Dijkstra, J. A. Kerr, and A. F. Trotman-Dickenson, *J. Chem. Soc., Sect. A*, 582 (1966).

Assuming $A_1 = A_2$

$$e^{(E_{12} - E_9)/RT}\frac{[NF_2Cl]}{[\cdot NF_2]} \geq 20$$

In similar manner

$$e^{(E_{13} - E_9)/RT}\frac{[NF_2Cl]}{[N_2F_4]} \geq 20$$

Using these values it is found that the activation energy differences, $E_9 - E_{12} \geq 1.6$ kcal and $E_9 - E_{13} \geq 1$ kcal, would account for the absence of ClCH₂CH₂NF₂ in the product.

It is apparent in the thermal reactions that there is more product derived from initiation of the reaction by addition of chlorine atoms to the olefin than from addition of the difluoramino radicals. This reflects the difference in activation energy of the two processes.[11] The difference between the thermal and photochemical reactions can be understood in terms of the comparative concentrations of difluoramino and chlorine radicals. In the presence of ultraviolet light at room temperature the chlorine atom concentration is high and the difluoramino radical low since tetrafluorohydrazine is not affected by light of these long wavelengths. Thermally the equilibrium between N₂F₄–Cl₂ and NF₂Cl can be established and at these temperatures the N₂F₄ is partially dissociated but the chlorine is not. These studies of chlorodifluoramine–olefin reactions complement very nicely those of the tetrafluorohydrazine–olefin reaction.[10,12]

Chlorodifluoramine and Mercurials

Chlorodifluoramine reacts with dimethyl-, diethyl- and di-*n*-butylmercury to produce a mixture of alkyl halide and alkyldifluoramine. However, from divinyl- and diphenylmercury only the organic halide was obtained. These reactions were conducted by stirring the liquid mercurial in an atmosphere of chlorodifluoramine for 5 to 48 hr. The halide–difluoramine mixture could be separated by gas chromatography. The alkyl

(11) The activation energy for the process Cl· + CH₂=CH₂ → ClCH₂CH₂· is estimated to be no greater than 1.4 kcal/mole: E. W. R. Steacie, "Atomic and Free Radical Reactions," Reinhold Publishing Corp., New York, N. Y., 1946, p 416.
(12) R. C. Petry and J. P. Freeman, *J. Org. Chem.*, in press.

chloride and alkyldifluoramine were produced in approximately equal amounts in all experiments, based on relative peak areas in the gas chromatogram of the combined fractions and the NF$_2$ balance for the experiments. The gas chromatogram of the n-butyl chloride–n-butyldifluoramine fraction from the di-n-butylmercury experiment showed a relative area ratio of 1:1.07 as compared to a relative ratio of 1:1.02 for a 1:1 mixture of the two compounds chromatographed under the same conditions. The data obtained for the aliphatic mercurials will be found in Table III in the Experimental Section.

Based on that data, the stoichiometry of these reactions closely approach that shown in eq 14. The rela-

$$3ClNF_2 + 2R_2Hg \longrightarrow N_2F_4 + RCl + RNF_2 + 2RHgCl \quad (14)$$
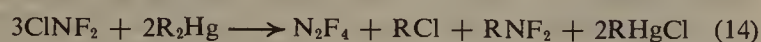
tive reactivity of the mercurials toward ClNF$_2$ appears to be n-butyl > ethyl >> methyl. In an experiment not reported in Table III, a mixture of ClNF$_2$ and excess dimethylmercury heated for 3 hr at 50° resulted in less than 10% reaction. Chromatography of the CH$_3$Cl–CH$_3$NF$_2$ fraction indicated approximately equal amounts of each were formed.

The mechanism of these reactions remains obscure. They apparently do not proceed by a free-radical path. In one experiment with diethylmercury, a 2:1 ratio of N$_2$F$_4$ to ClNF$_2$ was present at the start of the reaction. Although the stoichiometry was not measured in this case, the C$_2$H$_5$NF$_2$/C$_2$H$_5$Cl ratio (determined by gas chromatography) was not significantly different from that observed in the experiment reported in Table III. The result is not consistent with the formation of these products by the following competing reactions if one assumes equal solubility for N$_2$F$_4$ and ClNF$_2$ in the liquid mercurial. Also it is not known

$$R\cdot + NF_2Cl \longrightarrow RCl + \cdot NF_2$$

$$R\cdot + \cdot NF_2 \longrightarrow RNF_2$$

$$R\cdot + N_2F_4 \longrightarrow RNF_2$$
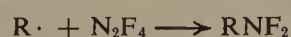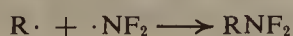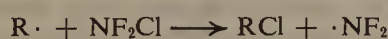
why no difluoramine was produced from divinyl- or diphenylmercury.

Reactions with Nucleophiles

A brief investigation of the reaction of chlorodifluoramine with some nucleophiles was made to determine if this reagent would function as a source of the difluoramino group. The principal reactions observed were of the redox type producing tetrafluorohydrazine and no particularly new chemistry was discovered.

Chlorodifluoramine is not attacked rapidly by aqueous base but is destroyed by ethanolic sodium ethoxide rapidly even at −80°. Tetrafluorohydrazine was recovered quantitatively. It is presumed that ethanol is oxidized during this process but no effort was made to isolate an organic product. The sodium salt of 2-nitropropane was oxidized to 2,3-dinitro-2,3-dimethylbutane. Sodium in liquid ammonia reduced NF$_2$Cl completely; all the fluorine was recovered as fluoride ion. Mercury reacts with chlorodifluoramine to produce N$_2$F$_4$ and mercurous chloride. These reactions may be generalized as

$$X^- + NF_2Cl \longrightarrow X\cdot + NF_2\cdot + Cl^-$$

Aniline and chlorodifluoramine reacted in the presence of β-naphthol to yield 1-benzeneazo-2-naphthol in fair yield. Although it is tempting to formulate this reaction as occurring through an N-difluoramino derivative which is dehydrofluorinated to the diazonium salt, there is actually no evidence aside from the product bearing on the mechanism of the reaction.

Summary

Chlorodifluoramine behaves as a source of chlorine and difluoramino radicals under the influence of heat and light. The product distribution from its thermal and photochemical reactions with olefins is fully consistent with previous studies involving difluoramino radicals alone. In addition ClNF$_2$ reacts with aliphatic mercurials to yield alkyldifluoramines. Toward strong nucleophiles ClNF$_2$ acts as an oxidizing agent and may be thought of as a source of positive halogen.

Experimental Section

Preparation of Chlorodifluoramine. A 1-l. Pyrex reagent bulb equipped with stopcock and condensing arm was charged in vacuo with 1.40 × 10^{-2} mole each of boron trichloride and difluoramine. The reactants were distilled into the reaction bulb with the condensing arm maintained at approximately −130° (methylcyclohexane slush bath temperature). The cooling bath was removed and the reaction mixture allowed to warm to ambient temperature. Reaction occurred below room temperature during the warm-up period and the bulb became coated with a white solid. The pressure in the reaction bulb corresponded to 2.0 × 10^{-2} mole of gaseous material at the completion of the reaction. Mass spectra and infrared analysis of the gaseous material showed the presence of NF$_2$Cl, HCl, and Cl$_2$, with small amounts of BCl$_3$ and BF$_3$. The solid nonvolatile reaction product was not identified, but appeared to contain the fluoroborate ion. The gaseous reaction mixture was separated by low-temperature vacuum fractionation through traps maintained at −130 and −196°. The −196° fraction contained the NF$_2$Cl contaminated with HCl and small amounts of Cl$_2$ and BF$_3$. Purification was accomplished by passage of this fraction through an Ascarite-packed tower at 0° and low pressure, followed by fractionation through a trap maintained at −130° to remove water. The passed fraction collected at −196° amounted to 6.96 × 10^{-3} mole (49.8% yield) and was essentially pure NF$_2$Cl.

An alternate purification method consisted of exposing the NF$_2$Cl fraction to 3 N sodium hydroxide solution (at room temperature) with stirring for 30 min, followed by fractionation through a trap at −130° to remove water. The physical properties, analysis, and characterization of chlorodifluoramine have been described.[3]

Olefin Addition Reaction. The conditions employed are found in Table II The reactions were conducted on a millimole scale in Pyrex bulbs by condensing in equimolar quantities of the olefin and NF$_2$Cl and heating the mixture in an oil bath at the temperature listed. The contents were then distilled on a vacuum line through traps at −80 and −196°. The contents of the −80° trap were then chromatographed on a dinonyl phthalate–chromosorb column to separate the components.

In the photochemical experiments the bulb was irradiated with a Hanovia EH-4 lamp at room temperature. The work-up was the same.

Reaction of ClNF$_2$ and Di-n-butylmercury. A 500-cc Pyrex reaction bulb equipped with stopcock and magnetic stirring bar was charged in vacuo with 2.2 g (0.0070 mole) of freshly distilled di-n-butylmercury and 0.0073 mole of pure ClNF$_2$. The reaction mixture was stirred at ambient temperature for 18 hr, during which time the pressure decreased from 228 to 170 mm and the formation of a white solid phase was observed. The reaction mixture was worked up by low-temperature vacuum fractionation through traps maintained at −24, −118, and −196°. There was no noncondensable fraction. The −196° fraction amounted to 0.0028 mole; quantitative infrared analysis showed 90% N$_2$F$_4$ and 10% ClNF$_2$. The −118° fraction weighed 0.46 g. Gas chromatography of the −118° fraction on a dinonyl phthalate column at 60° showed two components present in approximately equal amounts. These

Table III. Reaction of $ClNF_2$ with Dialkylmercury Compounds

Reactants, mmoles		Reaction conditions		Products, mmoles	RCl +		Recovered reactants, mmoles	
$ClNF_2$	R_2Hg	Time, hr	Temp, °C	N_2F_4	RNF_2	$RHgCl$	$ClNF_2$	R_2Hg
R = n-C$_4$H$_9$								
7.3	7.0	18	25	2.5	4.6	4.2	0.3	...[a]
5.1	~10	24	25	1.7	...[a]	...[a]	0.0	...[a]
R = C_2H_5								
7.1	7.1	4	25	2.2	4.0	(3.5)[b]	0.7	2.4
14.3	14.3	48	25	4.8	8.3	(5.3)[b]	0.0	...[a]
R = CH_3								
2.0	~3	5	80	0.71	1.4	...[a]	0.0	...[a]

[a] Size of fraction not measured. [b] Appreciable mechanical losses were sustained.

Table IV. N_2F_4–NF_2Cl–Cl_2 Equilibrium. Experimental Data for Mixture 4,[a] Table I

Equilibrium pressure, mm				Temp, °C
N_2F_4	Cl_2	$ClNF_2$	K	
45.1	451.1	9.86	0.00478	49.90
(44.9)	(450.9)	(10.18)	(0.00512)	
Repeat irradiation				
44.7	450.7	10.55	0.00552	
(45.1)	(451.1)	(9.86)	(0.00478)	
42.2	448.2	15.56	0.0128	69.70
(42.1)	(448.1)	(15.80)	(0.0132)	
Repeat irradiation				
42.4	448.4	15.32	0.0123	
(42.0)	(448.0)	(15.95)	(0.0135)	
39.1	445.6	21.75	0.0271	83.10
(39.0)	(445.0)	(22.00)	(0.0279)	
47.3	453.3	5.50	0.00141	29.00
(47.4)	(453.4)	(5.19)	(0.00125)	
45.9	451.9	8.15	0.00320	41.25
(46.1)	(452.1)	(7.90)	(0.00300)	
47.3	453.3	5.40	0.00136	33.25
(47.2)	(453.2)	(5.49)	(0.00141)	
Repeat irradiation				
47.1	453.1	5.81	0.00158	
(47.1)	(453.1)	(5.82)	(0.00158)	
Repeat irradiation				
47.1	453.1	5.80	0.00158	
(47.3)	(453.3)	(5.50)	(0.00140)	

[a] Mixture 4 initially contained 406 mm of Cl_2 and 100 mm of $ClNF_2$. Experiment made in order listed. The figures in parentheses indicate duplicate analyses.

were separated and trapped by gas chromatography and identified as n-butyl chloride (0.0025 mole) and n-butyldifluoramine (0.002 mole). The −24° fraction was found to be unreacted di-n-butyl-mercury. The nonvolatile white solid remaining in the reaction bulb was washed with pentane and filtered. There was thus obtained 1.22 g (0.0042 mole) of n-butylmercuric chloride, mp 127–128° (lit.[13] mp 130°). Elemental analysis showed no fluorine.

The n-butyldifluoramine, bp 72°, was characterized by mass, infrared, and nmr spectra (F^{19} resonance, −54.6 ϕ) and molecular weight determination (calcd, 109; found, 107.2). The yield was 28% based on $ClNF_2$ consumed.

Anal. Calcd for $C_4H_9NF_2$: C, 44.00; H, 8.25; N, 12.85. Found: C, 44.47; H, 8.44; N, 12.67.

Dimethyl- and diethylmercury similarly yielded methyl- and ethyldifluoramine which was identified by comparison of their physical and spectral properties with those of authentic samples.[14] Data on these reactions are compiled in Table III.

Reaction of Aniline and Chlorodifluoramine in the Presence of β-Naphthol. Into an evacuated U-tube containing 0.43 g (0.003 mole) of β-naphthol, 0.81 g (0.01 mole) of aniline, and 5 ml of benzene was condensed 67 ml (0.003 mole) of NF_2Cl. The contents were warmed to room temperature and darkened after stirring for 2 hr at room temperature. A mass spectrum showed that the vapor above the solution contained 2.6% N_2O, 6.4% NO, 0.8% SiF_4, and 2.6% N_2F_4; the rest was benzene. After removing the volatile components, the dark residue was taken up in benzene, washed with 10% sulfuric acid and water, and dried. The red solution was chromatographed through silica gel and concentrated to yield a red solid which was identified as 1-phenylazo-2-naphthol, mp 133–135° (lit.[15] mp 135°).

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Copper(II) and Samarium(III) Catalysis of the Hydrolysis of Ethyl Glycinate-N,N-diacetic Acid

Robert J. Angelici and Bruce E. Leach

Contribution from the Department of Chemistry, Iowa State University, Ames, Iowa 50010. Received March 30, 1967

Abstract: Ethyl glycinate-N,N-diacetic acid (EGDA) was prepared by the reaction of iodoacetic acid and glycine ethyl ester in basic solution and was identified by elemental analysis, nmr, and infrared spectra. Butyl glycinate-N,N-diacetic acid (BGDA) was prepared analogously and identified by nmr. These ligands coordinate strongly with copper(II) and samarium(III), but the extent of ester carbonyl coordination to the metal is uncertain. The rate of hydrolysis of the complexes to form metal nitrilotriacetic acid (NTA) complexes in the pH range 5.0–7.0 was studied and found to obey the following rate law: rate = $k[M(EGDA)][OH^-]$. These kinetic results suggest mechanisms in which a hydroxide ion attacks the carbonyl carbon of the ester which has to some extent coordinated to the copper(II) or samarium(III) in a prior equilibrium. The most probable mechanisms consistent with ionic strength dependence studies and hydroxyl complex formation constants are discussed.

Transition metal ions have long been known to promote the hydrolysis of α-amino acid esters.[1] The nature of the hydrolytic process is important because of the possible relationships to biological systems. Several mechanisms have been proposed.[1-6] Most explain the promoted hydrolysis by the assumption that polarization of the carbonyl group by the metal ion makes the carbonyl carbon more susceptible to nucleophilic attack. However, most of these studies do not indicate whether coordination of the ester in fact occurs through only the amino group or through both the amino group and the carbonyl oxygen. There is also uncertainty as to the identity of the nucleophile. Evidence for water and hydroxide attack as well as general base catalysis has been presented.

Determinations of a mechanism and treatment of the kinetics have been difficult because of the many labile complexes which result when an α-amino acid ester and a metal ion are placed in aqueous solution and the pH is varied. In general, one or two ester ligands may coordinate and these may form hydroxo complexes as well so that determination of the reactive species and their concentrations is difficult. In the presence of so many species it is nearly impossible to rule out contributions to the observed rate from species other than the mono-α-amino acid ester–metal complex.

A solution to the problem is to use relatively inert metal complexes[5] or to simplify the aqueous system under survey by minimizing prior ester equilibria.

With the latter in mind, a study of substituted iminodiacetic acids was begun. Iminodiacetic acid (IMDA) itself has a high first formation constant (log K_1 = 10.55)[7] with copper(II) and a relatively low second formation constant (log K_2 = 5.65). These values maximize the amount of Cu(IMDA) formed in near-neutral solutions. The present investigation utilizes the copper(II) and samarium(III) complexes of ethyl glycinate-N,N-diacetic acid and butyl glycinate-N,N-diacetic acid to elucidate the kinetics and mechanism of the hydrolysis of an amino acid ester derivative. The product of the reaction is the well-known metal complex of nitrilotriacetic acid (NTA).

complex I

$$+ \; C_2H_5OH \; + \; H^+ \quad (1)$$
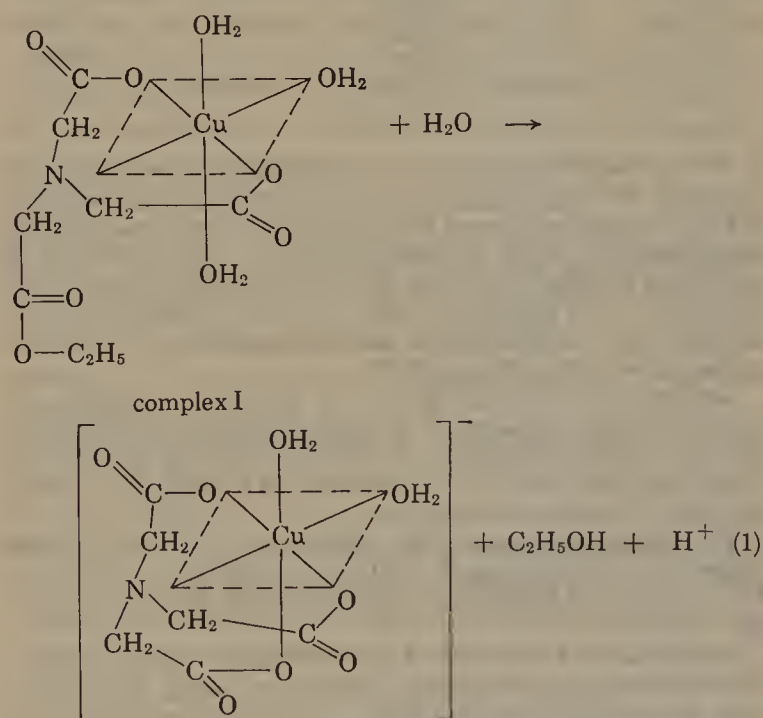
Experimental Section

Materials. Doubly distilled water and reagent grade $Cu(NO_3)_2 \cdot 3H_2O$ and KNO_3 were used in the kinetic studies. Samarium nitrate was a gift of Professor Jack Powell, Ames Laboratory. The concentration of Cu(II) in standard $Cu(NO_3)_2$ solutions was determined by thiosulfate titration of the iodine liberated from the reaction of KI with Cu(II). Samarium(III) was determined by titration with Na_2HEDTA using xylene orange indicator.[8,9] For the infrared spectral studies in D_2O, $Cu(NO_3)_2 \cdot 3D_2O$ was prepared by dissolving $Cu(NO_3)_2 \cdot 3H_2O$ in 99.5% D_2O and evaporating to dryness under vacuum. IMDA, methyliminodiacetic acid (Me-IMDA), and NTA used in nmr studies were reagent grade.

Preparation of $C_2H_5OOCCH_2N(CH_2COO)_2Ba$. Ethyl glycinate-N,N-diacetic acid was prepared by a modification of the general procedure given by Schwarzenbach[7] for substituted iminodiacetic acids.

(1) H. Kroll, *J. Am. Chem. Soc.*, **74**, 2036 (1952).
(2) M. L. Bender and B. W. Turnquest, *ibid.*, **79**, 1889 (1957).
(3) H. L. Conley, Jr., and R. B. Martin, *J. Phys. Chem.*, **69**, 2914 (1965).
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(9) J. Kinnunen and B. Wennerstand, *ibid.*, **46**, 92 (1957).

A 46.5-g portion (0.25 mole) of iodoacetic acid was dissolved in a minimum amount (~15 ml) of H_2O and chilled in an ice bath. Several drops of phenolphthalein indicator was added and a solution of NaOH added slowly with stirring. The temperature was kept below 30°. When the neutralization was complete, a solution of 17.6 g (0.125 mole) of glycine ethyl ester hydrochloride was added slowly. The pH was maintained at approximately 9 during the addition of the ester by addition of NaOH. After stirring the solution for 30 min at room temperature the product was precipitated by adding 31.8 g (0.26 mole) of $BaCl_2 \cdot 2H_2O$. The precipitate was filtered, washed with hot water, and dried.

For identification by nmr it was necessary to convert the barium salt which was only slightly soluble in water into the sodium salt. This was accomplished by adding Na_2SO_4, filtering the $BaSO_4$, and evaporating the resulting solution to dryness at room temperature under vacuum. The nmr spectrum was obtained on a Varian Associates Model HR-60 spectrometer in D_2O using sodium 2,2-dimethyl-2-silapentane-5-sulfonate as internal standard (chemical shift = 0.0). As will be discussed later the chemical shifts of the ligands are dependent upon the pH of the solution (see Table I).

Table I. Nmr of
$$CH_3—CH_2—O—\overset{\overset{\displaystyle O}{\displaystyle \|}}{C}—CH_2N(CH_2COONa)_2$$
$$\text{A} \qquad \text{B} \qquad \text{C} \qquad \text{D}$$

pD 5.90 δ, ppm	Rel intensity	Multiplicity	Assignment
1.28	3	Triplet (J_{H-H} = 6.8 cps)	A
4.30	2	Quartet (J_{H-H} = 6.8 cps)	B
3.86	2	Singlet	C
3.78	4	Singlet	D
3.47		Singlet	NTA

The nmr spectrum clearly identifies ethyl glycinate-N,N-diacetic acid, but the weak singlet at δ 3.47 indicates a small amount of NTA. Integration showed that 9% of the sample was NTA, the remaining 91% being the desired EGDA. Consistent with the purity was the observation that 89% of the sample undergoes ester hydrolysis. The presence of some NTA in the sample is not unexpected since at pH 9 of the preparation, EGDA was observed to undergo slow hydrolysis to NTA.

On the basis of the nmr results, the elemental composition was calculated for a mixture of 90 mole % ($C_2H_5OOCCH_2N(CH_2COO)_2Ba \cdot H_2O$) and 10 mole % ($HN(CH_2COO)_3Ba \cdot H_2O$). *Anal.* Calcd: C, 25.40; H, 3.42; N, 3.80; Ba, 37.13. Found: C, 25.45; H, 3.93; N, 3.99; Ba, 36.70.

The infrared spectrum of the mixture in a KBr pellet showed characteristic absorptions at 3440 (H_2O), 2960 (C–H), 1740 (ester C=O), 1570 and 1408 (salt of carboxylic acid), and 1210 and 1142 cm^{-1} (ester).

Preparation of $C_4H_9OOCCH_2N(CH_2COO)_2Ba$. Butyl glycinate-N,N-diacetic acid was prepared analogously using glycine butyl ester instead of glycine ethyl ester. Lanthanum nitrate was added to the barium salt of BGDA to form the lanthanum complex. The results of the nmr taken in D_2O are given in Table II.

Table II. Nmr of
$$[CH_3—CH_2CH_2—CH_2OOCCH_2N(CH_2COO)_2La]^+$$
$$\text{A} \quad \text{B} \quad \text{C} \qquad \text{D} \qquad \text{E}$$

pD 4 δ, ppm	Multiplicity	Assignment
0.90	Triplet	A
1.3–1.7	Multiplet	B
4.30	Triplet	C
3.82	Singlet	D
3.55	Singlet	E
3.47	Singlet	NTA

Kinetic Measurements. Rates of reaction were determined with a Radiometer TTT1c titrator and SBR2c titrigraph. The titrigraph plotted per cent volume of an SBU1a syringe buret. The titrator

was set for pH-stat work and the pH was maintained at the desired value by the addition of 0.0187 N NaOH. The standard 10-ml Radiometer thermostated reaction vessel was maintained at 25.0 ± 0.05°, and nitrogen was bubbled into the reaction vessel to exclude air. Radiometer electrodes and the standard stirrer were used.

A standard solution was prepared by adding 0.1480 g of the barium salt of EGDA to 62.5 ml of H_2O to make a 0.0067 M solution. For each kinetic run, 1.0 ml of 0.0067 M EGDA, 1.0 ml of 0.0067 M $Cu(NO_3)_2$, 2.5 ml of 0.2 M KNO_3, and 5.5 ml of H_2O were placed in the reaction vessel and thermostated for 15 min. The pH was raised to the desired value and the reaction followed automatically by the addition of NaOH solution while maintaining the given pH. One thus obtains a plot of the per cent of the total syringe capacity of NaOH solution delivered *vs.* time. Since the per cent at the end of the reaction (% end) minus the per cent at any time t (%t) is proportional to the concentration of unreacted EGDA, the slope of first-order plots of ln (% end − % t) *vs.* time, which are linear to at least 90% completion of reaction, yielded pseudo-first-order rate constants, k_{obsd}. Experimental and calculated % end values were identical if the known 90% purity of the ester was used and the pH was below the region of formation of appreciable amounts of hydroxo complexes. This is due to a difference in formation constants for Cu(EGDA)(OH) and Cu(NTA)(OH) or for the samarium analogs. Rate constants were almost always reproducible within ±10%. A general nonlinear least-squares computer program[10] was used to calculate the second-order rate constant, k, from the k_{obsd} and pH (*i.e.*, −log [a_H +]) data.

Rate Constants. The slope of a plot of ln (% end − % t) *vs.* time yields k_{obsd} from which the second-order rate constant, k, is obtained in activity units. All rate constants have been converted to molarity units by division by the appropriate factor (1.22 for 0.05 M ionic strength) calculated in the following manner:[11] pH* − pH = log y, where pH* = −log [H^+] and pH = −log a_H^+; log y is given by log y = $[-AZ_1Z_2I^{1/2}/(1 + I^{1/2})] + BI$, where I is the ionic strength and B is 0.1 for KNO_3.

Hydroxo-Complex Formation Constants. Hydroxo-complex formation constants, K_f, were determined at 25.0° for the MeIMDA and NTA complexes of Cu(II) and Sm(III) by titrating automatically with a Radiometer TTT1c titrator using 0.210 N NaOH and 0.05 M KNO_3 with a correction for NaOH consumed in a blank titration. The pH at the half-neutralization point was determined. Since the hydroxide activities, a_{OH^-}, were converted to concentrations, [OH^-], the K_f values are expressed in units of molarity. The calculated titration curve using the value of K_f, the hydroxo-complex formation constant, fits the experimental curve to within 10%.

Infrared Spectra. The infrared spectra obtained in 99.5% D_2O were made in 0.10-mm cells with Irtran-2 windows using a Beckman IR-12 grating spectrophotometer.

Results

The barium salt of ethyl glycinate-N,N-diacetic acid, [$C_2H_5OOCCH_2N(CH_2COO)_2Ba$], has been prepared and found to undergo immeasurably slow ester hydrolysis in the 4.5–7.5 pH range even in the presence of added Ba(II), but near pH 8 hydrolysis becomes significant. The pseudo-first-order rate constant, k_{obsd}, for hydrolysis at pH 9.5 is 2.0×10^{-4} sec^{-1}. Undoubtedly this includes contributions from several mechanisms of ester hydrolysis, probably including internal attack by $-COO^-$.[12] In the presence of copper(II) or samarium(III), however, hydrolysis is measurable in the 5.0–7.0 pH range. At higher pH values the rate of hydrolysis becomes too fast to measure by pH-Stat techniques.

From the known chelating tendencies of substituted iminodiacetic acids[6] it is certain EGDA is strongly coordinated to Cu(II) or Sm(III) through the iminodiacetic acid group to give complex I probably having a

(10) R. H. Moore, based on a report from Los Alamos Scientific Laboratory, LA 2367, plus addenda. We thank Mr. J. P. Birk for modification of this program for use on the present problem and computer facilities.

(11) S. W. Benson, "The Foundations of Chemical Kinetics," McGraw-Hill Book Co., Inc., New York, N. Y., 1960, pp 521–526.

(12) For a review on ester hydrolysis, see M. L. Bender, *Chem. Rev.*, 60, 53 (1960).

Table III. Summary of Chemical Shifts (cps) for MeIMDA and EGDA

| I. | MeIMDA, $CH_3N(CH_2COOH)_2$ | | | La^{+3} + $CH_3N(CH_2COOH)_2$ | | |
| | A B | | | A B | | |
pD	A	B	pD	A	B
2.40	181	240	3.00	179	233
3.05	179	232	4.50	177	228
4.05	177	227	5.58	170	222
7.00	177	227	6.70	152	205
8.35	176	225			
9.12	173	222			
12	134	183			

| II. | EGDA, $CH_3CH_2OOCCH_2N(CH_2COOH)_2$ | | | | $[La(CH_3CH_2OOCCH_2N(CH_2COO)_2)]^+$ | | | |
| | A B C D | | | | A B C D | | | |
pD	A	B	C	D	pD	A	B	C	D
4.00	77	259	234	228	5	77	259	224	211
5.90	77	259	232	227	5[a]	77	260	225	210
7.40	76	255	227	217					
9.50	74	259	209	195					

[a] Using sodium acetate buffer solution at pD 5.

structure as shown in eq 1. In this structure, the three donor atoms are shown to occupy meridional positions. While this configuration has been shown not to be preferred for cobalt(III) iminodiacetic acid complexes,[13] it is very probably adopted by Cu(II) which has a tendency to form square-planar complexes.

Of particular importance for the catalysis of the hydrolysis of EGDA is whether the ester carbonyl group is coordinated to the metal or not. In an attempt to clarify the situation, nmr studies were undertaken using a Varian Associates Model A-60 spectrometer. Attention was focused on the methylene in the $-NCH_2-$ $COOC_2H_5$ grouping. The chemical shifts of the uncoordinated ligand were studied as a function of pD to determine the pD range for the species $[C_2H_5OOCCH_2-N(H)(CH_2COO)_2]^-$ which has the same charge as $[CH_3N(H)(CH_2COO)_2]^-$, methyliminodiacetic acid (MeIMDA), the model compound which was selected for comparison with EGDA. The methylene of EGDA ($-NCH_2COOC_2H_5$) would be expected to show a downfield shift (provided the ester carbonyl oxygen is coordinated) upon coordination to a metal relative to the change in chemical shift of the methyl group in MeIMDA upon the coordination of MeIMDA to the same metal. Chemical shift parameters in cps were obtained for EGDA and MeIMDA both as free ligand and complexes with La(III). These results are given in Table III.

Lanthanum(III) was used because it forms the most soluble complexes of diamagnetic metal ions which catalyze the hydrolysis of EGDA. Considering the use of D_2O, a more valid measure of the acidity of the sample solutions was obtained by making use of an equation given by Mikkelson and Nielson:[14] pD = meter reading + 0.40.

One must first account for the change in chemical shifts with pD. If there are more than one species in solution, the nmr spectrum gives the time average of these species. To ensure that only one species is present, the pD must not be near the value of a pK_a. This is seen in Table III for MeIMDA. pD values of 2.40 and 3.05 are too near the pK_a of the acid protons (pK_a = 2.12) and the chemical shift values contain contributions

from $[CH_3N(H)(CH_2COOH)(CH_2COO)]$ as well as $[CH_3N(H)(CH_2COO)_2]^-$. The chemical shift values were relatively constant for MeIMDA in the pD 4–7 range, and this was taken to indicate a single species in solution. Titrations had previously established the presence of $(CH_3N(H)(CH_2COO)_2]^-$ in this pH range.[7] The values of the chemical shifts in this pD range were therefore taken for use in the comparison. At higher pD values (8–12) the hydrogen on the nitrogen is removed (pK_a = 9.65) and an upfield shift was observed with increasing pD. Similarly for EGDA, the chemical shift values are relatively constant between pD 4 and 6, and this was evidence for a single species in solution. The pK_a of the amino group in amino acid esters is about 2 pK_a units lower than that for amino acids,[15] and consequently it was observed that at a lower pD value (7.40) the chemical shifts due to the EGDA were already showing effects of proton removal from the nitrogen.

La(III) does not complex with MeIMDA at pD 3–4.5, and the chemical shifts were those expected due to free MeIMDA. The addition of excess La(III) at pK = 6.70 had no effect on the chemical shifts which implied that complexation was complete. Hence these values of chemical shifts due to $[La(MeIMDA)]^+$ were used in the comparison.

Utilizing the values in Table III for the particular pD at which the desired species exist, a comparison was made between the difference in chemical shift values of free and coordinated EGDA and the difference in chemical shift values between free and coordinated MeIMDA. For $[CH_3N(H)(CH_2COO)_2]^-$ chemical shifts of 177 and 227 cps for the methyl and methylene groups, respectively, were utilized. Upon coordination to form $La[CH_3N(CH_2COO)_2]^+$, the chemical shifts were 152 and 205 cps from the methyl and methylene groups, respectively. The upfield shift with coordination is due to the fact that La(III) is apparently not as strong an acid as H^+ in this system. EGDA values of chemical shifts are 77, 259, 232, and 227 from A, B, C, and D, respectively, for the species

$[CH_3CH_2OOCCH_2N(H)(CH_2COO)_2]^-$ (pH 4–6)
  A   B   C   D

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and, for the coordinated species (LaEGDA]$^+$ with corresponding assignments, the chemical shifts were 77, 259, 224, and 211 for the respective assignments A, B, C, and D.

It is to be noted that the chemical shifts of the methyl and methylene hydrogens of the ester function do not change on coordination. The $-N(CH_2COO^-)_2$ methylene protons of MeIMDA shift 21 cps upfield upon coordination, while the analogous protons in EGDA undergo a slightly smaller upfield shift (16 cps). Coordination with La(III) also produces upfield shifts in the CH_3 protons of MeIMDA (25 cps) and the $-NCH_2-COOC_2H_5$ methylene protons of EGDA (8 cps). If the $-COOC_2H_5$ group did not coordinate to the La-(III), it would be expected that the $-NCH_2COOC_2H_5$ methylene protons would shift upfield by roughly the same amount as observed for the CH_3 protons of MeIMDA. That the $-NCH_2COOC_2H_5$ protons do not shift as far upfield suggests that the ester group is losing electron density to La(III). While this interpretation of the shifts is not unambiguous, it does imply that some ester to La(III) bonding occurs.

In a further attempt to clarify the possibility of ester carbonyl coordination, the infrared stretching frequency in D_2O of the Cu(EGDA) complex was investigated. It has been established from solid-state infrared spectra of some amino acid ester complexes of Cu(II) that carbonyl coordination to Cu(II) lowers the carbonyl stretching frequency by about 100 cm^{-1}.[16] In the present study in the absence of Cu(NO$_3$)$_2$ and at a pD of about 7 the ester carbonyl absorption occurred at 1723 cm^{-1}, and the $-COO^-$ groups absorbed at 1603 cm^{-1}. Both frequencies are usual for the respective groups.[17] Upon addition of Cu(NO$_3$)$_2$ to the solution, the pD dropped to about 5 and the $-COO^-$ absorption shifted to 1636 cm^{-1} as expected for this group when coordinated to Cu(II).[17] The ester carbonyl absorption, however, broadens and its frequency shifts insignificantly to 1725 cm^{-1}. These results suggest that the predominant form of the complex present in solution before hydrolysis occurs is the metal complex of EGDA in which the ester group is not coordinated to the Cu(II) (structure I, eq 1). Because of the broadness of the ester carbonyl absorption of the La(III) complex of EGDA, it was impossible to determine any carbonyl stretching shift, although this broadness may itself suggest the presence of two absorptions corresponding to uncoordinated and coordinated ester. In general, however, the nmr and infrared spectral results do not allow us to unambiguously determine the amount of ester–metal coordination.

The product of the hydrolytic reaction is the metal complex of NTA. This was supported by the reaction stoichiometry and by noting that the ultraviolet–visible spectrum of the reaction solution using Cu(II) as the metal ion at infinite time was identical with that of a solution prepared from Cu(II) and NTA. The ester was also hydrolyzed in the presence of Zn(II), and the proton nmr gave a singlet at δ 3.65 ppm which was in good agreement with that found for a D_2O solution prepared from Zn(II) and NTA directly.

The pseudo-first-order rate constants, k_{obsd}, for reaction 1 at various pH values at 25.0° are given in Tables

(16) M. P. Springer and C. Curran, *Inorg. Chem.*, 2, 1270 (1963).

(17) Y. Tomita and K. Uneo, *Bull. Chem. Soc. Japan*, 36, 1069 (1963).

Table IV. Rates of Cu(II)-Catalyzed Hydrolysis of EGDA According to Eq 1[a]

pH	$10^4 k_{obsd}$, sec^{-1}	pH	$10^4 k_{obsd}$, sec^{-1}
5.50	0.684	6.50	6.15
5.80	1.21	6.60	8.78
6.10	2.48	6.80	12.3
6.30	3.91	7.00	23.2
6.40	4.92		

[a] At 25.0°, [Cu(II)] = [EGDA] = 0.00067 M; [KNO$_3$] = 0.050 M.

Table V. Rates of Sm(III)-Catalyzed Hydrolysis of EGDA According to Eq 1[a]

pH	$10^4 k_{obsd}$, sec^{-1}	pH	$10^4 k_{obsd}$, sec^{-1}
5.50	1.82	6.30	9.84
5.80	3.26	6.50	13.4
6.00	4.66	7.10	54.5

[a] At 25.0°, [Sm(III)] = [EGDA] = 0.00067 M; [KNO$_3$] = 0.05 M.

IV and V for Cu(II) and Sm(III), respectively. If k_{obsd} depends on the hydroxide ion concentration in the following manner, $k_{obsd} = k[OH^-]$, a plot of log k_{obsd} vs. pH will yield a straight line with a slope of 1.00. This was observed and the over-all rate of hydrolysis is then given by the expression

$$\text{rate} = k[\text{complex I}][OH^-]$$

where complex I is the Cu(II) complex of EGDA as shown in eq 1 or where Sm(III) is substituted for Cu(II) or BGDA for EGDA. The nonlinear least-squares evaluation of k yields a value of 2.18×10^4 M^{-1} sec^{-1} with a standard deviation of 0.07×10^4 M^{-1} sec^{-1} for Cu(II) and EGDA. The rates of hydrolysis of BGDA according to eq 1 at 25.0° with [Cu(II)] = [BGDA] = 0.00067 M and [KNO$_3$] = 0.05 M were determined at pH 6.30, 6.50, and 6.70 with values of $10^4 k_{obsd}$ (sec^{-1}) of 1.98, 2.90, and 4.97, respectively. The nonlinear least-squares evaluation of k yields a value of 9.75×10^3 M^{-1} sec^{-1} with a standard deviation of 0.03×10^3 M^{-1} sec^{-1}. For Sm(III) and EGDA the evaluation of k yields a value of 4.47×10^4 M^{-1} sec^{-1} with a standard deviation of 0.28×10^4 M^{-1} sec^{-1}.

The dependence of the rate of hydrolysis on the ionic strength of the medium was determined at pH 6.30 for the hydrolysis reaction involving Cu(II) and EGDA. Concentrations of KNO$_3$ of 0.025, 0.050, and 0.0100 M were used to give values of ionic strength, I (KNO$_3$ + Ba(II) from BaEGDA), of 0.028, 0.053, and 0.103 M. Values of $10^4 k_{obsd}$ (sec^{-1}) at these respective ionic strengths were 3.86, 3.90, and 3.78, which are the same within experimental error. Replacement of KNO$_3$ with KCl has no effect. The corresponding study with Sm(III) and EGDA with values of ionic strength of 0.003, 0.028, 0.053, 0.103 and 0.203 M gave values of 10^4_{obsd} (sec^{-1}) of 10.9, 8.90, 9.81, 7.20, and 5.84, respectively. A plot of log k_{obsd} vs. $\sqrt{I}/(1 + \sqrt{I})$ gave a straight line of slope 1.04.

A medium of high dielectric constant stabilizes charged species, and the effects can be predicted by considering the following reaction.
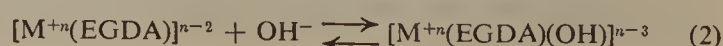
$$[M^{+n}(EGDA)]^{n-2} + OH^- \rightleftharpoons [M^{+n}(EGDA)(OH)]^{n-3} \quad (2)$$

Mechanism A[18]

$$\xrightleftharpoons{K} \qquad \xrightarrow{\dfrac{k_{OH}}{OH^-}} \qquad \text{fast}$$

Cu(NTA)$^-$ + C$_2$H$_5$OH
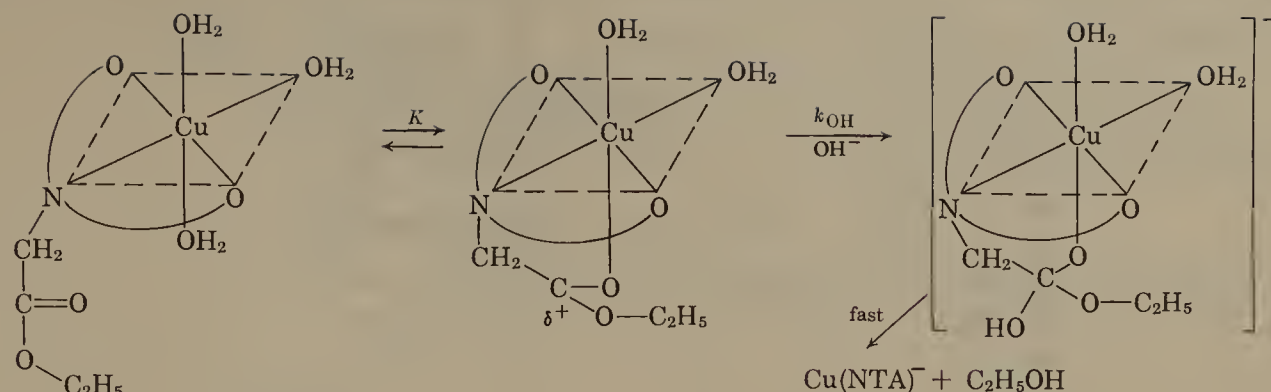
Equation 2 corresponds to formation of a hydroxo complex or an intermediate. For Cu(II) and EGDA, the Cu(EGDA) complex is neutral and the left side of eq 2 contains a singly charged particle (OH$^-$). The right side of eq 2 also bears a single charge, so that neither side of the equation is favored by changing the ionic strength, and indeed no effect was observed. For Sm(III) there are two unit charged species on the left and a neutral species on the right side of eq 2, and therefore the charged species should be stabilized by increasing ionic strength and the observed rate constant k_{obsd} should decrease as was observed. Quantitatively $\log k_1/k_0 = -A\Delta(Z)^2\sqrt{I}/(1 + \sqrt{I})$, where $A = 0.507$ for aqueous solutions and $\Delta(Z)^2$ is defined as usual as the charges on products minus reactants (i.e., $(n - 3)^2 - (1)^2 - (n - 2)^2$ for eq 2).[11]

Excess Cu(II) ion had no effect on the rate of hydrolysis. With a concentration of 0.00067 M EGDA and increasing the concentration of Cu(II) from 0.00067 to 0.0011 to 0.0015 M, the pseudo-first-order rate constants (3.90, 3.68, and 3.65 $\times$ 10^{-4} sec^{-1}, respectively) remained, within experimental error (<10%), unchanged. Also adding Sm(III) up to a 1:1:1 ratio of Cu:EGDA:Sm had no effect on the copper-catalyzed rate constant consistent with the higher formation constants of Cu(II) with the model compounds (IMDA or NTA). The addition of excess Sm(III) to the Sm(III)-catalyzed hydrolysis reaction of EGDA had no effect within the limits of experimental error on the rate even for [Sm(III)] = 0.00134 M and [EGDA] = 0.00067 M. Using a deficiency of metal the rate of hydrolysis was that expected for the particular concentration of complex I. However, after the complexed ester had hydrolyzed, the reaction continues at a much slower rate until all the ester had been hydrolyzed. The slow terminal hydrolysis was presumably a result of some complexation with excess EGDA instead of NTA by the metal ion. Addition of other chelating groups such as glycine to a solution of Cu(EGDA) slowed the rate of hydrolysis presumably by complexation.

The formation constants of hydroxo complexes of Sm(III) and Cu(II) with MeIMDA and NTA were determined. EGDA itself hydrolyzed in the pH range where hydroxo complexes form, and no accurate formation constants could be obtained. However, it would be expected that the hydroxo formation constants of metal EGDA complexes would be bounded by the values of the hydroxo complex formation constants for MeIMDA and NTA, depending on the extent of the ester carbonyl oxygen coordination. Values of K_f = [M(L)(OH)]/[ML][OH$^-$] for L = MeIMDA or NTA were as follows (±5%): Cu(MeIMDA)(OH), K_f =

6.4 $\times$ 10^5; Cu(NTA)(OH), K_f = 8.2 $\times$ 10^4; Sm-(MeIMDA)(OH), K_f = 6.4 $\times$ 10^6; Sm(NTA)(OH), K_f = 2.0 $\times$ 10^6.

Discussion

The kinetic study of reaction 1 shows that the rate of reaction depends on the concentration of complex I and hydroxide ion. It is very likely that complex I, however, may not be the reactive form of the ester, but rather a complex in which the carbonyl oxygen of the ester is coordinated with Cu(II) or Sm(III). The existence of such an intermediate is supported by the work of Alexander and Busch.[5] They found that an amino acid ester which is coordinated to Co(III) only through the amino group hydrolyzes very slowly, but, when coordinated through both the amino group and the carbonyl oxygen, hydrolysis proceeds quite rapidly. The absence of the detection of such an intermediate in the current work does not eliminate the possibility of such an intermediate being present in very low concentrations. Alexander and Busch also observed general nucleophilic catalysis, and external nucleophilic attack on the carbonyl carbon was postulated. A similar mechanism written for Cu(II) catalysis of the hydrolysis of EGDA is Mechanism A which involves rate-determining hydroxide ion attack on the carbonyl carbon which has been polarized by coordination to the metal ion in a rapid prior equilibrium to yield NTA metal complex and ethyl alcohol. This mechanism gives the rate law: rate = Kk_{OH}[complex I][OH$^-$] and is consistent with the observed rate law and ionic strength dependence. K, the equilibrium constant for coordinated carbonyl ester oxygen, is probably small but indeterminable. An infrared study in D$_2$O of Cu(II) and ethyl glycinate showed no evidence for ester carbonyl oxygen coordination to Cu(II) so that an indeterminable constant K is involved for Cu(II)-catalyzed hydrolysis of ethyl glycinate as well.[2-4]

There is, however, another mechanism which is kinetically indistinguishable in which the hydroxo complex [Sm(EGDA)(OH)] or the copper analog is the reactive species (Mechanism B). Formation constants of hydroxo complexes are large enough so that appreciable concentrations (approximately 0.01–20%) of Sm(EGDA)(OH) or Cu(EGDA)(OH)$^-$ exist in solution in the pH range 5.0–7.0. The hydroxide ion in the complex is in a position which makes possible an attack of hydroxide ion perpendicular to the plane of the carbonyl and ester bond as postulated by Bender.[12] The formation constants of hydroxo complexes of metal

(18) Catalysis by Sm(III) would involve eight- or nine-coordination rather than octahedral as shown for Cu(II).

Mechanism B [18]
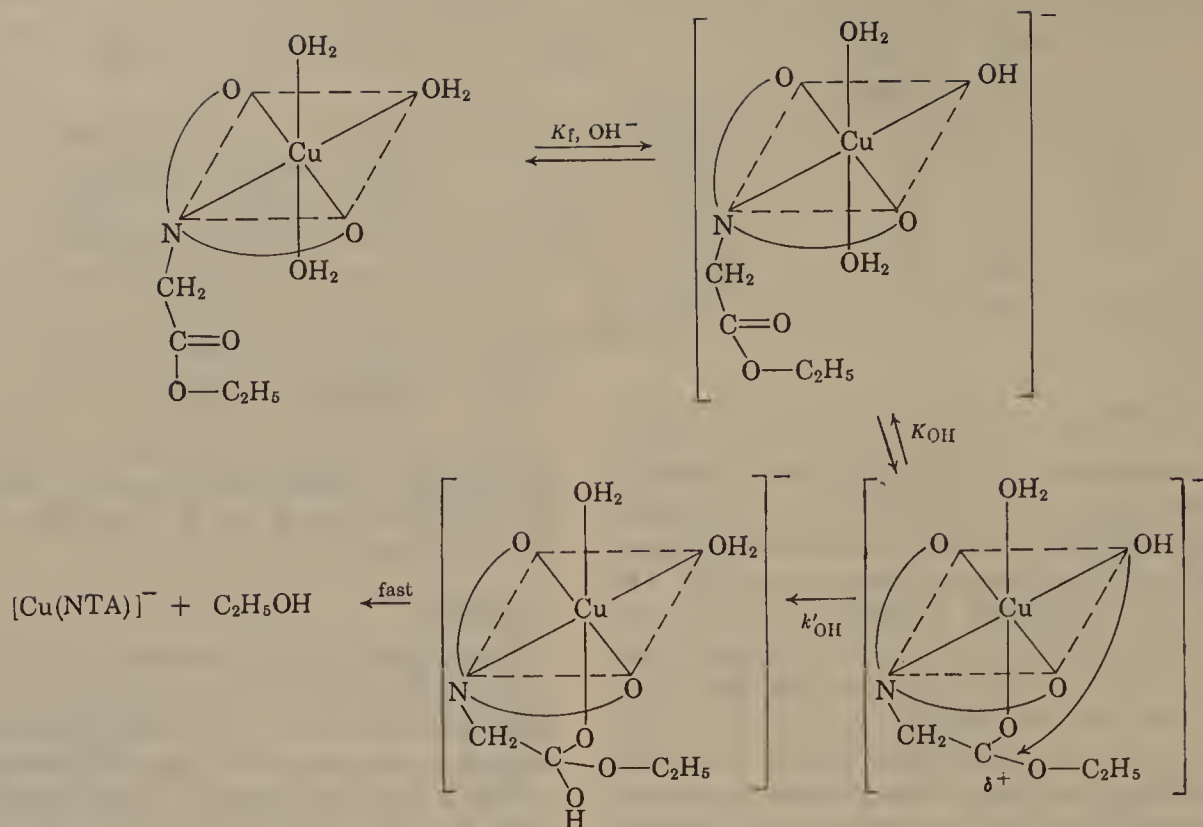
ions have been found to parallel the order found for hydrolytic rate constants for metal–ethyl glycinate complexes,[19] and preliminary work with other metal complexes of EGDA indicates this generalization may be applied in the present situation. This mechanism need not involve full coordination of the ester carbonyl to the metal, as suggested by the drawing. It is also possible that there is weak or no direct interaction between the carbonyl group and the metal. In any case, mechanism B gives a rate law of the form

$$\text{rate} = K_{OH}K_f k'_{OH}[\text{complex I}][\text{OH}^-]$$

No second-order hydroxide ion term was detected even at pH 7.0 so that hydroxide ion attack on an hydroxo complex may be eliminated. Water attack on a negatively charged or neutral species Cu(EGDA)(OH)$^-$ or Sm(EGDA)(OH) would seem unlikely since no water attack is observed for the neutral and positively charged complexes, Cu(EGDA) or Sm(EGDA)$^+$.

The problems of interpretation due to the unknown values of K and K_{OH}, the equilibrium constants for ester carbonyl oxygen coordination, and the possibility of either external or internal hydroxide ion attack are common to metal-catalyzed hydrolysis of amino acid esters and their derivative unless coordination of the ester carbonyl can be proven and the absence of hydroxo complexes established. Literature values for the rates of hydroxide ion catalyzed hydrolysis of various amino acid esters and their metal complexes are tabulated in Table VI. The rate constants for Cu(EGDA)^0 and

Cu(NH$_2$CH$_2$COOEt)$^{+2}$ are surprisingly similar in view of the formal charges of zero and $+2$ on the respective complexes.

Table VI. Rate Constants for Hydroxide Ion Catalyzed Hydrolysis Reactions of Amino Acid Esters and Derivatives at 25°

Ester	k_1, M^{-1} sec^{-1}	Ref
NH$_2$CH$_2$COOEt	0.635	15 ($I = 0.1$)
$^+$NH$_3$CH$_2$COOEt	24	3 ($I = 0.16$)
(C$_2$H$_5$)$_3$N$^+$CH$_2$COOEt	20.8	15
Cu(NH$_2$CH$_2$COOEt)$^{+2}$	7.6 × 10^4	3
Cu(EGDA)	2.18 × 10^4	This work
Sm(EGDA)	4.47 × 10^4	This work
Cu(BGDA)	9.75 × 10^3	This work

The decrease in the rate of hydrolysis of the butyl ester (BGDA) by a factor of 2.2 compared to the ethyl ester (EGDA) is somewhat larger than that observed for basic hydrolysis of organic acetates (1.18)[20] but is in good agreement with the rate of hydrolysis of butyl glycinate (0.305 M^{-1} sec^{-1})[21] compared to that of ethyl glycinate (0.635).[15]

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Proton Magnetic Resonance Spectra of Platinum(II) Complexes. I. Pyramidal Configuration and Inversion at Sulfur in cis-Bis(dibenzyl sulfide)dichloroplatinum(II). Temperature and Solvent Effects on AB Chemical Shifts[1-3]

Paul Haake and Patricia Cronin Turley

Contribution No. 2071 from the Department of Chemistry, University of California, Los Angeles, California 90024. Received March 14, 1967

Abstract: Nuclear magnetic resonance spectra of cis-bis(dibenzyl sulfide)dichloroplatinum(II) indicate that in the ground state the sulfur atoms are pyramidal. Dynamic structure is also found: the sulfur atoms invert with a rate constant of 10.3 sec^{-1} at 34.5°, and the inversion process does not involve dissociation of the Pt–S bond. The activation energy, E_a, required for inversion at sulfur is 18.0 kcal/mole; the logarithm of the frequency factor is 13.8. These results come from study of the methylene region of the nmr spectra. The methylene resonance was proven to be an AB (66.3% due to Pt with $I = 0$) + ABX (33.7% due to ^{195}Pt with $I = 1/2$) pattern by three experiments: double irradiation, inducement of a double-quantum transition, and amplification of the normal spectrum with a time-averaging computer. The two vicinal platinum–proton coupling constants are 29.3 and 55.7 cps at 35°. The AB chemical shift in this complex and in dibenzyl sulfoxide is dependent on temperature and solvent polarity.

The compound under study in this paper is cis-bis-(dibenzyl sulfide)dichloroplatinum(II) (**2**). It is well known that platinum(II) complexes are planar, leading to the possibility of cis and trans isomers. But there are important structural questions beyond that. Which rotamers are favored in rotation about carbon–sulfur and sulfur–platinum bonds? What is the configuration at sulfur? If sulfur is pyramidal as in sulfoxides, how fast is inversion? Is there any barrier to rotation about sulfur–platinum bonds? This paper provides some experimental evidence bearing on these questions.

Although many metal–organosulfur complexes are known, there are very little structural data available. Crystallographic studies indicate that in a diethyl sulfide–mercury complex[4] and a nickel mercaptide polymer[5] the sulfur atom is pyramidal. In solution, recent nmr studies[3,6] show that sulfur is pyramidal when bonded to platinum and palladium. Moreover, inversion at sulfur is much faster than in sulfoxides[7-10] and sulfonium ions.[11] A study by Abel, Bush, Hopton,

and Jenkins[6] involved a sulfur chelate (**1**). In **1**, inversion at sulfur could occur by breaking one S–Pt bond and re-forming it with the other configuration at sulfur.

This paper describes in detail the nmr behavior of cis-bis(dibenzyl sulfide)dichloroplatinum(II) (**2**). The dependence of the AB chemical shift (nonequivalent methylene protons) of **2** on temperature and solvent polarity is compared with that of the corresponding system in dibenzyl sulfoxide (**3**).
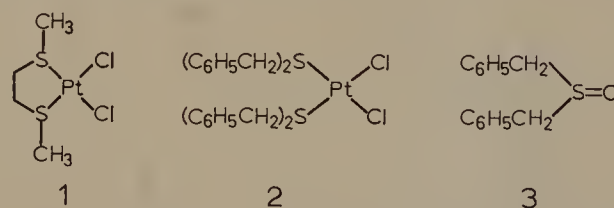
Experimental Section

Nmr Spectra. The nmr spectra were recorded with two Varian A-60's, one of which was equipped with a variable-temperature probe, and a Varian HR-60 equipped with a temperature probe and a frequency-sweep unit. Spectra were calibrated by the side-band technique[12] using Hewlett–Packard 200AB or 200CD wide-range oscillators and a Hewlett–Packard 5233L frequency counter. Chemical shifts were measured relative to internal tetramethylsilane.

Preparation of cis-Bis(dibenzyl sulfide)dichloroplatinum(II). A mixture of benzyl sulfide and K_2PtCl_4 (mole ratio 3:1) in water was shaken for 24 hr. The solid was filtered off and triturated with benzene. Evaporation of the benzene extract produced the yellow complex which was recrystallized from acetone several times; decomposition occurs at 150–157° (lit.[13] 150°).

Anal. Calcd for $C_{28}H_{28}Cl_2PtS_2$: C, 48.40; H, 4.06. Found: C, 48.53; H, 4.31. Infrared: two broad Pt–Cl bands at 324 and 314 cm^{-1}.

Preparation of Dibenzyl Sulfoxide. Dibenzyl sulfide was oxidized with sodium metaperiodate in 50% aqueous ethanol according to Leonard and Johnson's method,[14] mp 132–133°.

(1) Dedicated to the late Dr. A. J. R. Bourn.

(2) Research supported in part by Grant GP-3726 from the National Science Foundation, by Grant AM-6870 from the U. S. Public Health Service, and by an Alfred P. Sloan Research Fellowship to P. H.

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Results

The probe temperature proton magnetic resonance spectrum of **2** (methylene region only) is shown in Figure 1a. The methylene protons are represented by five peaks having a mean chemical shift at -230 cps. The large, closely spaced doublet integrates for four times the area of the single downfield peak. The separation between the most upfield and the most downfield peaks is 50 cps, and the midpoint falls within the "center" doublet. The distance between the second upfield peak and the single downfield peak is 36 cps with a midpoint coinciding with the downfield half of the center doublet. Since 33.7% of naturally occurring platinum is ^{195}Pt ($I = \frac{1}{2}$), the spectrum can be interpreted as an ABX (34%) pattern superimposed upon an AB (66%) pattern with J_{AX} ($\sim$50 cps) $\neq J_{BX}$ ($\sim$36 cps).
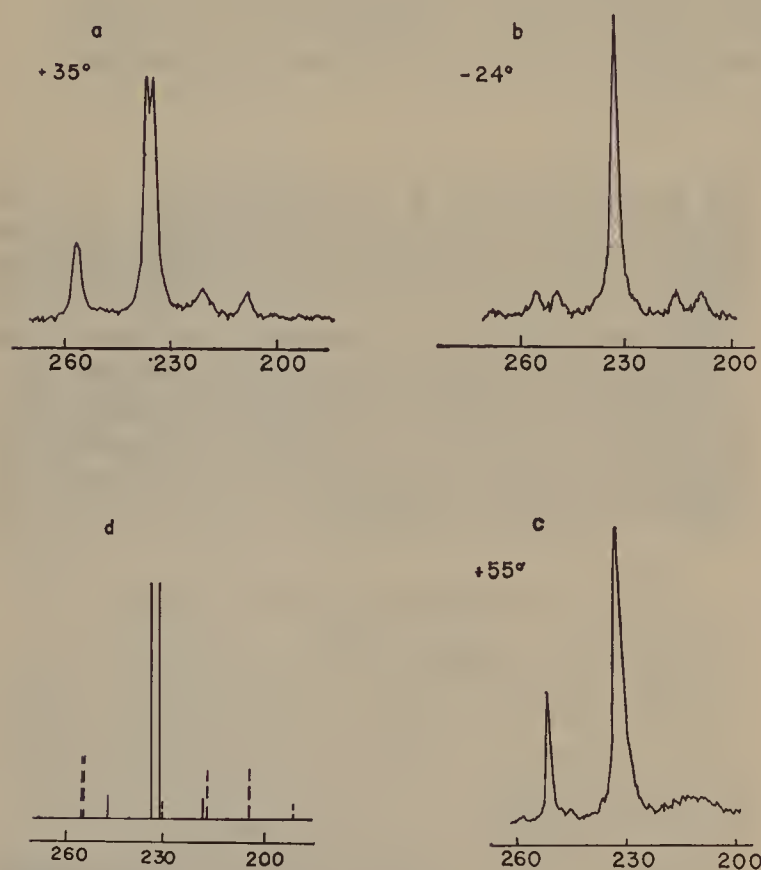
Figure 1. Methylene region of nmr spectra of *cis*-bis(dibenzyl sulfide)dichloroplatinum(II) (**2**): (a) at normal probe temperature; (b) at $-24°$; (c) at $+55°$; (d) calculated spectrum for AB (———, 66.3%) and ABX (– – – –, 33.7%).

Lowering the temperature causes the downfield platinum satellite to split into two broad peaks as is shown in Figure 1b. The center doublet collapses to a singlet although the methylene protons must still be nonequivalent since there are four platinum satellites. Raising the temperature produces coalescence; Figure 1c (55°) is near the coalescence temperature for the upfield satellites, although the center absorption is a fairly sharp singlet at this temperature. The single platinum proton coupling at 55° is ±43.0 cps, the average of the two frequency separations found at lower temperatures.

These nmr observations can be explained by an AB system caused by a pyramidal sulfur and the molecular environment shown in **4**. An averaging process such

as inversion would produce an A_2 system as is observed at higher temperatures. However, some of the signals predicted for the AB region in an AB + ABX system[12] are not observed, so this explanation cannot be confirmed from the spectra.

$$C_6H_5CH_2-\overset{\cdot\cdot}{\underset{R}{S}}\cdots Pt$$

4
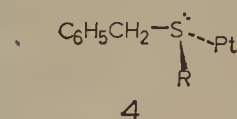
There are two other possible explanations which do not require the presence of more transitions than those observed. (1) The methylene groups could be nonequivalent because of restricted rotation about the Pt–S bond. Models make steric inhibitions to rotation seem unlikely, but double bond character caused by d–d π bonding in the square-planar complex (the filled platinum d orbitals are not all degenerate) might be involved.[15] (2) There could be two different sulfide groups caused by a distorted square-planar geometry,[16] but this seems unlikely.

Three methods have been used to detect hidden resonances and demonstrate the presence of an A–B system. First, we have utilized the effects of indirect spin–spin interactions. Figure 2 records the pmr spectra of the methylene protons of **2** when subjected to weak irradiation according to the method of Freeman
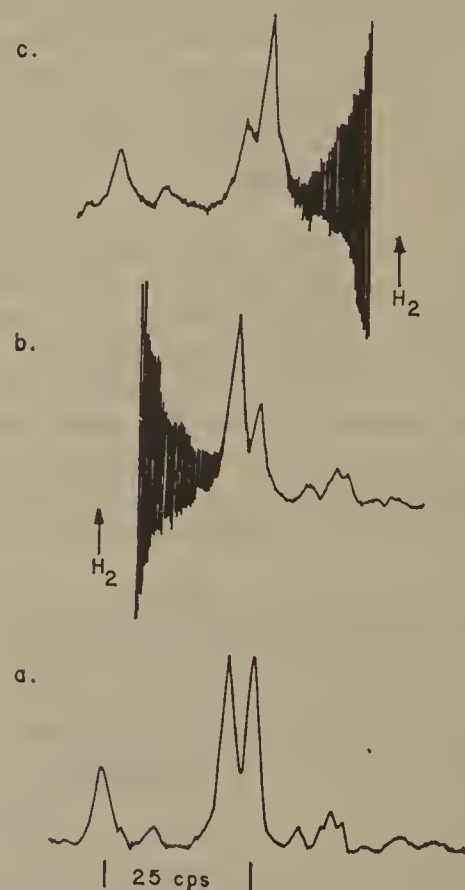
Figure 2. Methylene region in nmr spectrum of *cis*-bis(dibenzyl sulfide)dichloroplatinum(II) (**2**); $+11.8°$; solvent is CHCl$_3$–C$_6$H$_5$NO$_2$ (1:1). Some impurity peaks are present (see Figure 1a): (a) frequency-sweep spectrum; (b) irradiation of low-field side of center doublet; (c) irradiation of high-field side of center doublet.

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(16) F. Basolo and R. G. Pearson, *Progr. Inorg. Chem.*, **4**, 381 (1962).

and Anderson.[17] The alteration in line shape of the center doublet is due to irradiation of the weak hidden, outer resonances of the center AB quartet.[17] The transition regressive to the irradiated transition is not cleanly split as is often true,[17] probably because the magnitude of splitting is proportional to the square root of the intensity of the irradiated line.[17,18] The irradiated lines are very weak in this case, and only broadening of the regressive transition is observed.[19]

Secondly, a technique has recently been developed for assigning progressive transitions in an energy-level diagram.[18] If the radiofrequency power is increased until single-quantum transitions saturate and double-quantum transitions begin to appear, then the frequencies of the double-quantum transitions must correspond closely to the average of two progressively related single-quantum transitions. This method is applicable to the dibenzyl sulfide complex. The two energy diagrams (AB + ABX) constructed from the results of the double-resonance experiment predict double-quantum transitions at about -233 cps for the AB system and at -255 and -211 cps for the ABX system in the proton spectrum. Figure 3 shows the dependence of the pmr spectra of the methylene protons
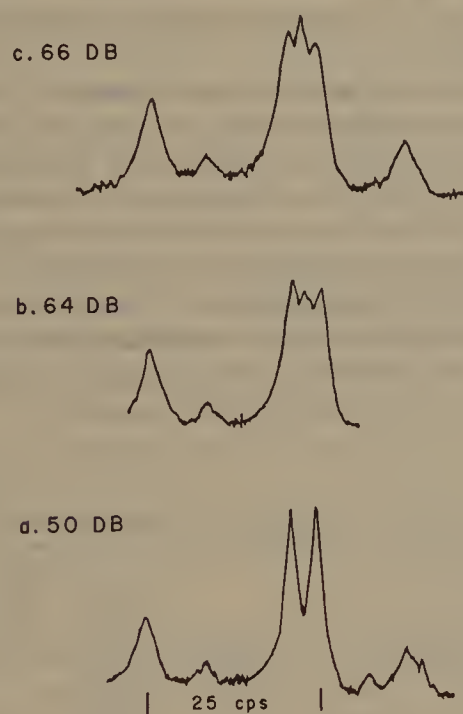
Figure 3. Double-quantum transitions in the nmr spectra of the methylene region of cis-bis(dibenzyl sulfide)dichloroplatinum(II) (2). Some impurity peaks are present (see Figure 1a): (a) normal spectrum with radiofrequency = 50 db; (b) radiofrequency = 64 db; (c) radiofrequency = 66 db.

upon radiofrequency power; one of the predicted double-quantum transitions was observed. Its existence and position is in agreement with the proposed AB system.

(17) (a) R. Freeman and W. A. Anderson, J. Chem. Phys., 37, 2053 (1962); (b) ibid., 39, 806 (1963).

(18) W. A. Anderson, R. Freeman, and C. A. Reilly, ibid., 39, 1518 (1963).

(19) Alternatively, the decreased intensity could be due to a transmission of saturated protons from the irradiated site to the observed site by the inversion process.[20a] The nuclear Overhauser effect seems less likely.[20b] All of these possibilities support an AB explanation for the nmr spectra of 2.

(20) (a) S. Forsen and R. A. Hoffman, J. Chem. Phys., 39, 2892 (1963); (b) K. Kuhlmann and J. D. Baldeschwieler, J. Am. Chem. Soc., 85, 1010 (1963).

Thirdly, the Varian time-averaging computer was used and a low-intensity peak was observed at -191 cps corresponding to an outer peak of the upfield AB system. This experiment enabled a more accurate determination of the geminal coupling constant. A final, theoretical, computed spectrum (Figure 1d) gave agreement with all observations using the following parameters (cps): $\Delta\nu_{AB} = 8.4$, $J_{AB} = -13.0$, $J_{AX} = 55.7$, $J_{BX} = 29.3$.

Rate Process. A temperature dependence of the methylene protons in 2 was observed (Figure 1c). Above $55°$, only one 1:4:1 methylene system is observed, indicating rapid exchange of protons between the A and B sites leading to an A_2 system. This exchange could occur by inversion at sulfur. Exchange of ligands would lead to loss of Pt–S–C–H coupling (still present in Figure 1c), so this cannot explain the observations at higher temperature. The spectra can be broken down into three AB patterns corresponding to platinum spins of $+\frac{1}{2}$, 0, and $-\frac{1}{2}$, and the AB group furthest downfield will be assigned arbitrarily to $I_{Pt} = +\frac{1}{2}$. A graph of temperature vs. chemical shift separation is shown in Figure 4. The least-
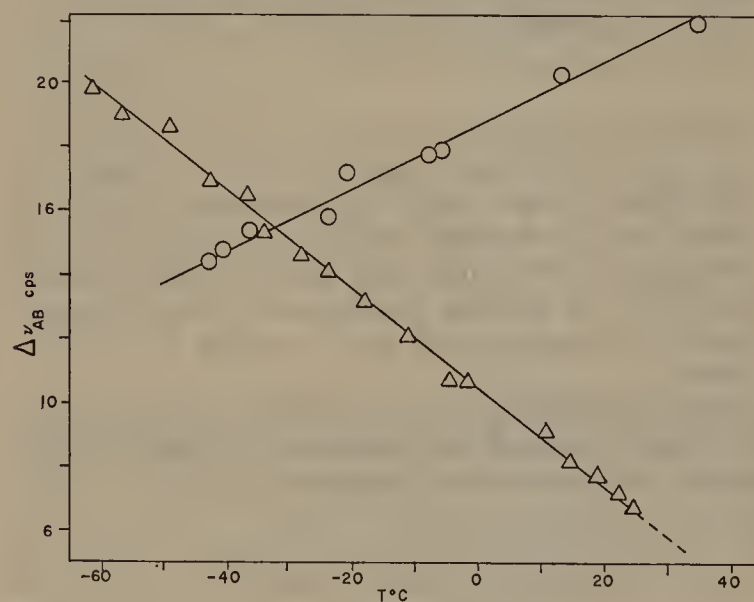
Figure 4. Dependence of chemical shift on temperature in cis-bis(dibenzyl sulfide)dichloroplatinum(II): △, downfield AB system; ○, upfield AB system.

squares equations for cps separation between A and B protons are for $I_{Pt} = +\frac{1}{2}$ and $T = -62$ to $+25°$

$$\Delta\nu_{AB}^+ = \nu_B^+ - \nu_A^+ = -0.153T + 10.41 \quad (1)$$

$$\sigma_{slope} = 0.002 \quad \sigma_{intercept} = 0.08$$

and for $I_{Pt} = -\frac{1}{2}$ and $T = -43$ to $+13°$

$$\Delta\nu_{AB}^- = \nu_A^- - \nu_B^- = 0.106T + 18.92 \quad (2)$$

$$\sigma_{slope} = 0.007 \quad \sigma_{intercept} = 0.18$$

The temperature range in which the peak separation of the center AB pattern could be determined experimentally was quite small; therefore, the net $\Delta\nu_{AB}$ for 2 was determined from the data displayed in Figure 4 and eq 1 and 2.

$$\Delta\nu_{AB} = \nu_A - \nu_B = (\nu_A^+ + \nu_A^- - \nu_B^+ - \nu_B^-)/2 =$$
$$(\Delta\nu_{AB}^- - \Delta\nu_{AB}^+)/2 = 0.130T + 4.26 \quad (3)$$
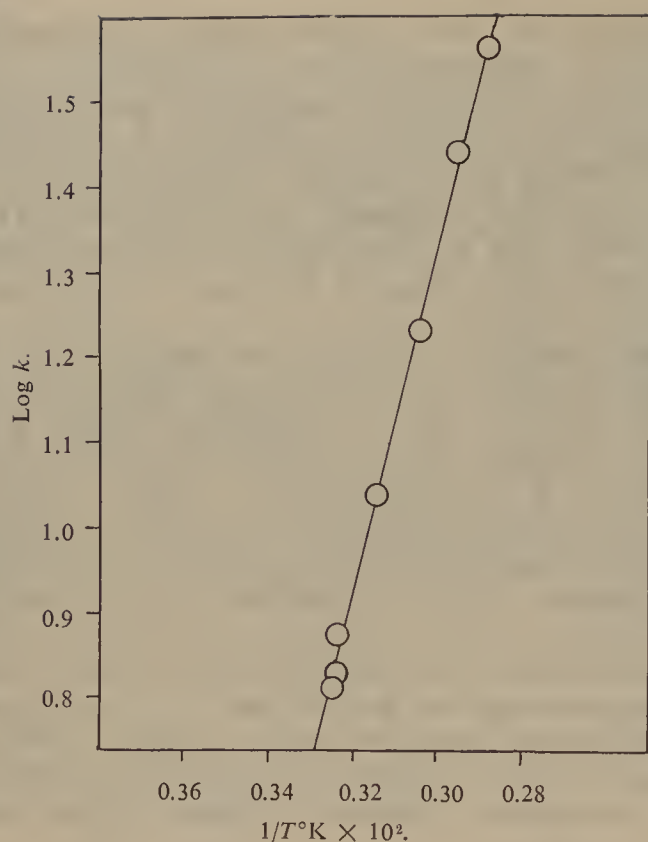
Figure 5. Arrhenius plot of the rate of sulfur inversion in *cis*-bis(dibenzyl sulfide)dichloroplatinum(II).

Note that temperature for eq 1–3 is in °C. Therefore $\Delta\nu_{AB}$ (eq 3) becomes negative at $\sim -33°$ (Figure 4). These linear relationships,[21] in the absence of exchange, allow the true AB chemical shifts to be obtained at any temperature within the valid range of the equations. The three AB systems coalesce at different temperatures, permitting several rate constants to be determined.

At a peak separation, $\Delta\nu_e$, sufficiently different from the actual chemical shift separation, $\Delta\nu$, the rate constant, k, for inversion was calculated from[23]

$$k = \frac{\pi}{\sqrt{2}}(\Delta\nu^2 - \Delta\nu_e^2)^{1/2} \qquad (4)$$

At coalescence eq 4 reduces to

$$k = \pi\Delta\nu/\sqrt{2} \qquad (5)$$

Above the coalescence temperature, the peak width, W^* (in cps), was used to evaluate the rate constant for the averaging process[23b]

$$k = \frac{\pi\{W'' + W^*[1 + 2(W^*/\Delta\nu)^2 - (W^*/\Delta\nu)^4]^{1/2}\}}{2[(W^*/\Delta\nu)^2 - (W''/\Delta\nu)^2]} \qquad (6)$$

where W'' = line width at half-maximum signal amplitude in the absence of exchange, W^* = observed line

(21) Although an exponential rather than a linear relationship would be expected ($\Delta\nu = \sum_i a_i\Delta\nu_i e^{-E_i/RT}$), it has been shown[22] in substituted ethanes that the curvature is small. Over a 100° temperature range, a straight line is a reasonable approximation of the actual curve.

(22) H. S. Gutowsky, G. G. Belford, and P. E. McMahon, *J. Chem. Phys.*, 36, 3353 (1962).

(23) (a) H. S. Gutowsky and C. H. Holm, *ibid.*, 25, 1228 (1956); (b) A. Allerhand, H. S. Gutowsky, J. Jonas, and R. Meinzer, *J. Am. Chem. Soc.*, 88, 3185 (1966).

width at half-height. When $W^* \gg W''$, eq 6 reduces to

$$k = \frac{\pi}{2}\Delta\nu[(\Delta\nu/W^*)^2 - (W^*/\Delta\nu)^2 + 2]^{1/2} \qquad (7)$$

The free energy of activation, ΔF^*, was calculated from rate constants determined by this method and from the Eyring equation (eq 8). The activation

$$\Delta F^* = 2.3RT[\log (B/h) + \log T - \log k] \qquad (8)$$

energy, E_a, was calculated from the Arrhenius relationship (eq 9). The enthalpy and entropy values were

$$2.3 \log k = -E_a/RT + 2.3 \log A \qquad (9)$$

calculated from

$$\Delta H^* = E_a - RT \qquad (10)$$

$$\Delta S^* = (\Delta H^* - \Delta F^*)/T \qquad (11)$$

An Arrhenius plot is shown in Figure 5. Therefore, the activation parameters for inversion at sulfur in **2** are: $\Delta F^* = 16.6 \pm 0.3$ kcal/mole, $E_a = 18.0 \pm 0.5$ kcal/mole, $\log A = 13.8 \pm 0.3$, $\Delta S^* = 3$ eu, $\Delta H^* = 17.4$ kcal/mole. The rate constant for inversion is 10.3 sec^{-1} at 34.5°.

Comparison of Sulfoxide and Complex. In order to learn more about the meaning of these observations on **2**, dibenzyl sulfoxide, a compound with similar configuration at sulfur, was studied. We investigated the effects of both temperature and solvent on $\Delta\nu_{AB}$ in **2** and **3**. Unfortunately the low solubility of *cis*-{[(C$_6$H$_5$CH$_2$)$_2$S]$_2$PtCl$_2$} sharply limited the choice of solvents. The dependence of the AB chemical shift is shown in Table I. In complex **2**, the geminal coupling constant is assumed to be -13.0 cps in all solvents.

Table I. Effect of Solvent on the AB Chemical Shifts

Solvent	ϵ	—3— $\Delta\nu$, cps	—3— J_{AB}, cps	—2— $\Delta\nu$,[e] cps
Carbon tetrachloride	2.24[a]	<2.0		
Chloroform	5.05[a]	<2.0		8.4
Nitrobenzene + chloroform (1:1)	21[b]	7.4	12.7	11.7
Nitrobenzene	36.1[a]	9.5	13.0	15.8
Cyanobenzene	25.2[c]	9.8	13.0	16.5
Nitromethane	37.5[a]	11.7	13.1	
Dimethyl sulfoxide	48.9[d]	16.3	13.0	
Dimethylformamide	36.7[a]	17.4	13.1	

[a] "Handbook of Chemistry and Physics," 46th ed, Chemical Rubber Co., Cleveland, Ohio, 1965. [b] Average of the dielectric constants of nitrobenzene and chloroform. [c] A. A. Maryott and E. R. Smith, National Bureau of Standards Circular No. 514, U. S. Government Printing Office, Washington, D. C., 1951. [d] H. L. Schlafer and W. Schaffernicht, *Angew. Chem.*, 72, 618 (1960). [e] J_{AB} assumed to be 13.0 cps in all solvents.

A temperature study of dibenzyl sulfoxide was carried out to see if there was dimeric association at low temperatures[24] and if there was inversion at high temperatures. A plot of the chemical shift between the methyl-

(24) R. F. Watson and J. F. Eastham, *ibid.*, 87, 664 (1965).

ene protons as a function of temperature is shown in Figure 6. No decrease in chemical shift between A and B protons was observed as the temperature was lowered in any solvent studied. Furthermore, as the temperature of the chloroform sample was raised, a gradual change from an A_2 to an AB system was not found. Therefore, we have found no evidence for dimerism[24] and inversion.[25]

Discussion

Pyramidal Sulfur and the Averaging Process. The results of double-irradiation experiments and the detection by time-averaging of an outer peak of an AB system demonstrate that the magnetic nonequivalence in Figure 1 is due to AB methylene groups. Therefore, the sulfur atom in **2** must be pyramidal so that only one pair of electrons on sulfur participates in σ bonding to the platinum atom. This structural result extends the crystallographic observations on sulfide–metal compounds.[4,5] The results obtained in this study give no evidence for hindered rotation about the S–Pt bond. Since studies were carried to $\sim-60°$, this places some limits on the possible barrier to rotation about this ligand–metal bond.

The averaging process which makes the two methylene hydrogens equivalent (on the nmr time scale) must be due to inversion at sulfur. Since we continue to observe Pt–S–C–H coupling above the coalescence temperature and the J above coalescence equals the average of the J's below coalescence, the inversion process cannot involve dissociation of the sulfide ligand, for that would lead to exchange of sulfides and loss of Pt–S–C–H coupling. The activation entropy for the inversion process is within experimental error of zero as expected for a symmetrical, unimolecular reaction.[26]

Dibenzyl Sulfoxide. We examined dibenzyl sulfoxide (**3**) as a simple model for the more complex platinum(II) compounds. Both **2** and **3** have pyramidal sulfur atoms and both have π back-bonding because of d–d overlap in **2** and p–d overlap in **3**.

Solvent Effects on $\nu_A - \nu_B$. The data in Table I and Figure 6 demonstrate a pronounced increase in $\Delta\nu_{AB}$ for **3**, with increase in dielectric constant and decrease in temperature. Association may be important, since it has been reported that this leads to a negligible $\Delta\nu_{AB}$ in sulfoxides.[24] In the more polar solvents, association would occur to a smaller extent. The changes in $\Delta\nu_{AB}$ may also be dependent on conformational populations involved in rotation about the C–S bond, the orientation and anisotropy of the phenyl rings, and the anisotropy of the S=O bond.

Conformational studies have indicated that the lone pair of electrons on nitrogen has a preference for the equatorial position similar to that of a hydrogen or perhaps smaller.[27] In cyclic sulfoxides, the pair of electrons on sulfur apparently has a greater preference for the equatorial position than the sulfoxide oxygen.[28]

(25) Inversion rates of sulfoxides have been measured polarimetrically [D. R. Rayner, E. G. Miller, P. Bickart, A. J. Gordon, and K. Mislow, *J. Am. Chem. Soc.*, **88**, 3138 (1966)] and are very much slower than required for observation by nmr.

(26) The mechanism of inversion is discussed fully in the accompanying paper: P. C. Turley and P. Haake, *ibid.*, **89**, 4617 (1967).

(27) (a) K. Brown, A. R. Katritzky, and A. J. Waring, *Proc. Chem. Soc.*, 257 (1964); (b) P. J. Brignell, A. R. Katritzky, and P. L. Russell, *Chem. Commun.*, 723 (1966).
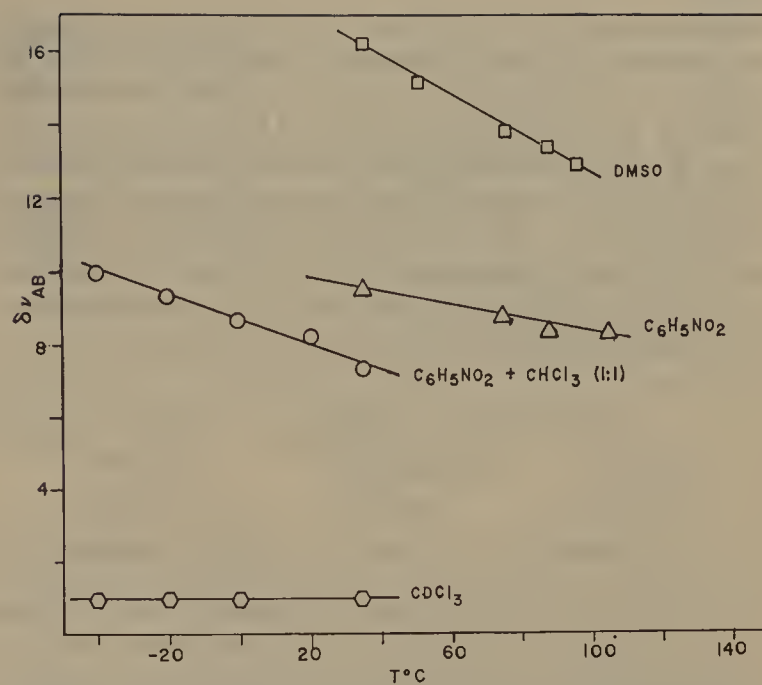
Figure 6. Temperature dependence of $\Delta\nu_{AB}$ for the methylene groups of dibenzyl sulfide.

If these results can be extended to acyclic systems, the order of stabilities should be $5 > 6 > 7$ for the conformations about the S–C bond on the right-hand side of those drawings.[29]
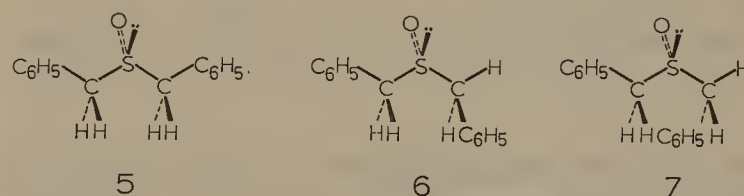
In **5**, the two benzyl hydrogen atoms are in different positions, *gauche* and *trans*, with respect to the S=O bond. The S=O bond has been treated in several ways to derive its diamagnetic anisotropic effect.[30] In some six-membered ring sulfoxides, treatment of the S=O bond as a triple bond has explained observed chemical shifts of nearby hydrogens.[30c]

It has been shown in benzyl ethers that $\Delta\nu_{AB}$ is dependent on orientation of the phenyl ring of the benzyl group.[31] However, in those studies[31] $\Delta\nu_{AB}$ decreased with increasing dielectric constant, but we have found the reverse (Table I). In **5**, the difference in size of the sulfur, oxygen, and unshared pair could cause a different orientation of the phenyl ring with respect to the two hydrogens.

The decreased $\Delta\nu_{AB}$ in **3** with increasing temperature may be due to a change in the distribution of conformational populations or to the decrease in dielectric constant with increasing temperature.

***cis*-Bis(dibenzyl sulfide)dichloroplatinum(II).** In **2**, conformational populations need to be considered for

(28) C. R. Johnson and D. McCants, Jr., *J. Am. Chem. Soc.*, **86**, 2935 (1964); J. C. Martin and J. J. Uebel, *ibid.*, **86**, 2936 (1964).

(29) Since it is not known why oxygen prefers the axial position in six-membered ring sulfoxides,[28] it is uncertain if **6** is preferred over **7**.

(30) (a) J. G. Pritchard and P. C. Lauterbur, *J. Am. Chem. Soc.*, **83**, 2105 (1961); (b) Y. Y. Samitov and R. M. Aminova, *J. Struct. Chem.* (USSR), **5**, 497 (1964); (c) K. W. Buck, A. B. Foster, W. D. Pardoe, M. H. Qadir, and J. M. Webber, *Chem. Commun.*, 759 (1966).

(31) (a) G. M. Whitesides, D. Holtz, and J. D. Roberts, *J. Am. Chem. Soc.*, **86**, 2628 (1964); (b) G. M. Whitesides, J. J. Grocki, D. Holtz, H. Steinberg, and J. D. Roberts, *ibid.*, **87**, 1058 (1965).

rotation about both C–S and S–Pt bonds. The steric requirements of the platinum group in **2** make it difficult to predict the preferred conformation for rotation about S–CH$_2$ bonds. Although the S–Pt bond is long (probably about 2.2 Å[32]), the S–Pt–S and S–Pt–Cl bond angles of 90° could make the Pt group sterically large. Models indicate that this is correct, and it appears impossible for all S-benzyl groups to be in conformation **8** at one time, but conformations **8** and **10** should certainly be the favored ones.
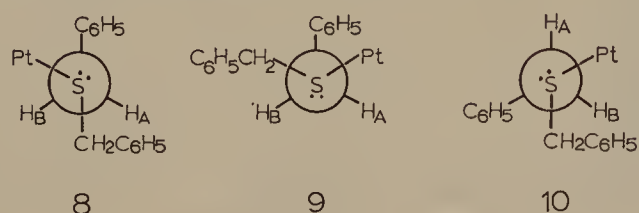
Relative sizes of groups indicate that the conformations shown in **11** and **12** should be favored in rotation about the S–Pt bond. These conformations minimize benzyl–benzyl and benzyl–chloro interactions that appear severe in rotated versions of **11** and **12**. The
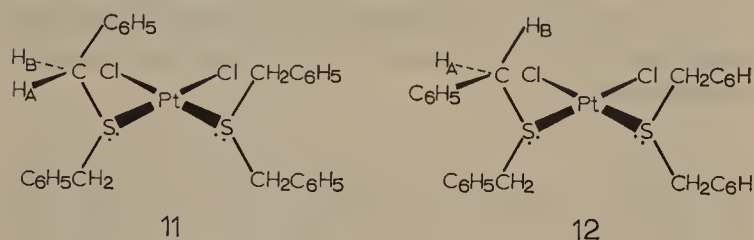
two favored conformations for rotation about the S–C bonds are shown in **11** (conformation **8**) and **12** (conformation **10**).

Temperature Effects on Coupling Constants in 2. Since the absolute values of the slopes in eq 1 and 2 are different, the platinum proton coupling constants also vary with temperature. If eq 1 and 2 are added, $J_{AX} - J_{BX}$ is obtained as a function of temperature.

$$J_{AX} - J_{BX} = (J_A{}^+ - J_A{}^-) - (J_B{}^+ - J_B{}^-) =$$
$$-0.047T + 29.33 \quad (12)$$

Conformation **8** should have the greatest difference in coupling constants in the two preferred conformations, **8** and **10**, because in **10**, but not in **8**, both hydrogens are *gauche* to platinum. The negative slope of eq 12 requires that the population of **10** increase with increasing temperature.

Temperature Effects on Chemical Shifts in 2. Solvents with higher dielectric constant result in increased $\Delta\nu_{AB}$ for **2** as is true for **3**. Temperature effects have been studied only in deuteriochloroform for **2**, but the dependence on temperature (eq 1–3 and Figure 4) has a negative slope; $\Delta\nu_{AB}$ decreases with increasing temperature.

An important factor in chemical shifts should be the relation of the hydrogen to the plane of the platinum complex. From the screening anisotropy in square-planar platinum(II) complexes, a methylene proton out of the plane is expected to be shifted downfield relative to one closer to the plane of the complex.[33] Therefore, it is important to consider rotation about the S–Pt bond.

In **11** (conformation **8**), there should be little contribution to $\Delta\nu_{AB}$ from the platinum anisotropy[33] since H$_A$ and H$_B$ are in similar positions with respect to the plane of the platinum complex. In **12** (conformation **10**), however, H$_B$ should be shifted downfield by the platinum anisotropy. Since the population of this conformer must increase with temperature (from coupling constants), the chemical shifts are in agreement with the proton assignments shown in **11** (**8**) and **12** (**10**). Therefore, we conclude that for Pt–S–C–H couplings, as in many other cases, $J_{trans} > J_{gauche}$. The consistency of this conclusion with other systems supports our proton assignments.

(32) Based on the Pt–P bond length in a phosphine–platinum(II) complex: R. Eisenberg and J. A. Ibers, *Inorg. Chem.*, 4, 773 (1965).

(33) A. D. Buckingham and P. J. Stevens, *J. Chem. Soc.*, 4583 (1964).

Proton Magnetic Resonance Spectra of Platinum(II) Complexes. II. cis- and trans-Bis(dialkyl sulfide)dichloroplatinum(II) Complexes. Mechanism of Inversion at Sulfur and Vicinal Platinum–Proton Couplings[1,2]

Patricia Cronin Turley and Paul Haake

Contribution No. 2072 from the Department of Chemistry, University of California, Los Angeles, California 90024. Received March 14, 1967

Abstract: The proton magnetic resonance spectra of several platinum–sulfide complexes have been studied at various temperatures. The rates of inversion at pyramidal sulfur are reported for cis- and trans-$[(R_2S)_2PtCl_2]$ complexes with three different sulfide ligands. trans complexes invert considerably more rapidly than cis complexes. Inversion at sulfur in these complexes is about 10^{18} times faster than inversion at sulfur in sulfoxides. The data are consistent with a mechanism for inversion in which the sulfur retains a distorted tetrahedral configuration and the platinum atom forms σ bonds alternately with the two sulfur lone pairs. The ratio of platinum–proton coupling constants (Pt–S–C–H) is fairly constant: $J_{trans}/J_{cis} = 0.82$. The sensitivity of the coupling interaction to the nature of the trans ligand is discussed.

In the preceding paper we have reported studies of the nmr spectra of **1**.[3] The methylene region was proven to be an AB (66%) + ABX (34%) system, sensitive to solvent and temperature as well as sulfur inversion. This paper describes observations by nmr on a series of cis and trans platinum(II) complexes (**1–8**). The results enable us to propose a mechanism for inversion at sulfur, and we discuss some factors affecting platinum–proton couplings.
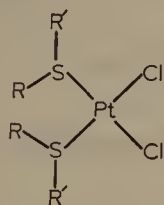
1, R = R′ = C₆H₅CH₂
3, R = R′ = CH₃CH₂
5, R = CH₃; R′ = C₆H₅CH₂
7, R = R′ = CH₃
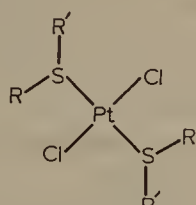
2, R = R′ = C₆H₅CH₂
4, R = R′ = CH₃CH₂
6, R = CH₃; R′ = C₆H₅CH₂
8, R = R′ = CH₃

Experimental Section

Nmr Spectra. The nmr spectra were recorded with two Varian A-60's, one of which was equipped with a variable-temperature probe, and a Varian HR-60 equipped with a temperature probe and a frequency-sweep unit. Spectra were calibrated by the side-band technique[4] using Hewlett–Packard 200AB or 200CD wide-range oscillators and a Hewlett–Packard 5233L frequency counter. Tetramethylsilane (TMS) was used as the internal standard. Rates of inversion and activation parameters were determined as previously described.[3]

Preparation of cis- and trans-Bis(dimethyl sulfide)dichloroplatinum(II). An attempt to prepare pure cis complex as described by

Cox[5] resulted in a cis (83%) and trans (17%) isomeric mixture as determined by their nmr spectra (see Results section).

Preparation of trans-Bis(diethyl sulfide)dichloroplatinum(II). Kauffman's method was used,[6] mp 104–105° (lit.[6] 107°).

Anal. Calcd for $C_8H_{20}Cl_2PtS_2$: Pt, 43.72. Found: Pt, 43.21. One Pt–Cl stretching vibration was found at 342 cm⁻¹ in the far-infrared spectrum as expected for a trans complex.[7]

Preparation of cis-Bis(diethyl sulfide)dichloroplatinum(II). Kauffman's method was used,[6] mp 104–105° (lit.[6] 107°).

Anal. Calcd for $C_8H_{20}Cl_2PtS_2$: Pt, 43.72; C, 21.52; H, 4.52. Found: Pt, 43.68; C, 21.73; H, 4.69.

Two Pt–Cl bands at 314 and 330 cm⁻¹ were found in the far-infrared as expected for a cis complex.[7]

Preparation of cis-Bis(methyl benzyl sulfide)dichloroplatinum(II). A mixture of K_2PtCl_4 (2 g, 0.005 mole) dissolved in 25 ml of water and methyl benzyl sulfide (2.07 g, 0.015 mole) in 10 ml of methanol was shaken for 12 hr. Yellow crystals were filtered off and recrystallized from hot aqueous ethanol to give fine yellow needles, mp 157–159°.

Anal. Calcd for $C_{16}H_{20}Cl_2PtS_2$: Pt, 36.00; C, 35.45; H, 3.72. Found: Pt, 35.95; C, 35.60; H, 3.86.

Two Pt–Cl bands at 324 and 318 cm⁻¹ were found in the far-infrared.

Results

Bis(dibenzyl sulfide)dichloroplatinum(II) Complexes. The detailed study of the cis complex is in the previous paper.[3] Above 25° a 1:4:1 set of signals appears in the CDCl₃ solution of the cis complex which is assigned to the trans isomer on the basis of chemical shift and coupling constant.[8] When the solution is cooled, these signals disappear indicating a reversible, temperature-dependent isomerization. Since at 27° the 1:4:1 signal from **2** shows no magnetic nonequivalence as observed for **1**,[3] a limit can be set on the rate of inversion at sulfur in **2** (Table I).

Bis(diethyl sulfide)dichloroplatinum(II) Complexes. Figures 1–3 record the nmr spectra of the methylene

(1) Dedicated to the late Dr. A. J. R. Bourn.

(2) Research supported by Grant GP-3726 from the National Science Foundation, by Grant AM-6870 from the U. S. Public Health Service, by a grant from the Faculty Research Committee of U.C.L.A., and by an Alfred P. Sloan Research Fellowship to P. H. A preliminary report of this work has appeared: P. Haake and P. C. Turley, *Inorg. Nucl. Chem. Letters*, **2**, 173 (1966).

(3) P. Haake and P. C. Turley, *J. Am. Chem. Soc.*, **89**, 4611 (1967).

(4) J. A. Pople, W. G. Schneider, and H. J. Bernstein, "High Resolution Nuclear Magnetic Resonance," McGraw-Hill Book Co., Inc., New York, N. Y., 1959.

(5) E. G. Cox, H. Saenger, and W. Wardlaw, *J. Chem. Soc.*, 182 (1934).

(6) G. B. Kauffman and D. O. Cowan, *Inorg. Syn.*, **6**, 211 (1960).

(7) P. Haake, G. Hurst, and K. Stark, unpublished results.

(8) A. Pidcock, R. E. Richards, and L. M. Venanzi, *Proc. Chem. Soc.*, 184 (1962); *J. Chem. Soc., Sect. A*, 1707 (1966).

Table I. Activation Parameters for Inversion in Platinum–Sulfur Compounds

Compound[a]	T_c, °K[b]	k_T, sec^{-1}[c]	Log A, sec^{-1}[d]	E_a, kcal/mole[d]	ΔF^*, kcal/mole[e]	ΔH^*, kcal/mole	ΔS^*, eu
cis-[(C$_6$H$_5$CH$_2$)$_2$S]$_2$PtCl$_2$ (1)	307.5	10.3	13.8[f]	18.0[f]	16.6[f]	17.4	3
trans-[(C$_6$H$_5$CH$_2$)$_2$S]$_2$PtCl$_2$ (2)	<300	>10^2			<15		
cis-[(C$_2$H$_5$)$_2$S]$_2$PtCl$_2$ (3)	333	64.7			16.8		
trans-[(C$_2$H$_5$)$_2$S]$_2$PtCl$_2$ (4)	274	36.4			13.9		
cis-(CH$_3$SCH$_2$C$_6$H$_5$)$_2$PtCl$_2$ (5)	309	11.6	14.8[g]	19.2[g]	16.5	18.6	7
trans-(CH$_3$SCH$_2$C$_6$H$_5$)$_2$PtCl$_2$ (6)	<223	>50			<12		

[a] Solvent was CDCl$_3$ except for **5** where it was CH$_2$Cl$_2$. [b] Coalescence temperature = T_c. [c] Rate of inversion at coalescence temperature = k_T. [d] Arrhenius parameters for $k = Ae^{-E_aRT}$. [e] Estimated probable error is ±0.3 kcal/mole. [f] Standard deviations: $\sigma_{E_a} = 0.5$ kcal/mole; $\sigma_{\log A} = 0.3$. [g] Standard deviations: $\sigma_{E_a} = 1.1$ kcal/mole; $\sigma_{\log A} = 0.8$.

protons of **3** and **4** at various temperatures. The lack of symmetry in the resonance below the coalescence temperatures indicates there are two different platinum proton coupling constants in each complex. In **4**, coalescence of the center and most intense portion of the ABM$_3$ system ($I_{Pt} = 0$) occurs at +1 ± 5° (Figure 2b); in **3**, coalescence of the center multiplet to an A$_2$M$_3$ system occurs at +60 ± 5° (Figure 3b).
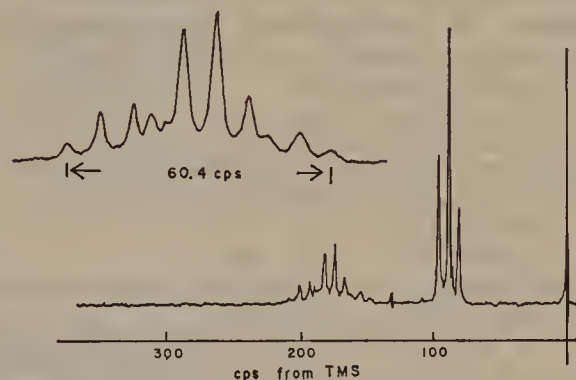
Figure 1. Nmr spectrum of *trans*-bis(diethyl sulfide)dichloroplatinum(II) in CDCl$_3$ at normal probe temperatures (about 30°); upper trace is an enlargement of the methylene region.
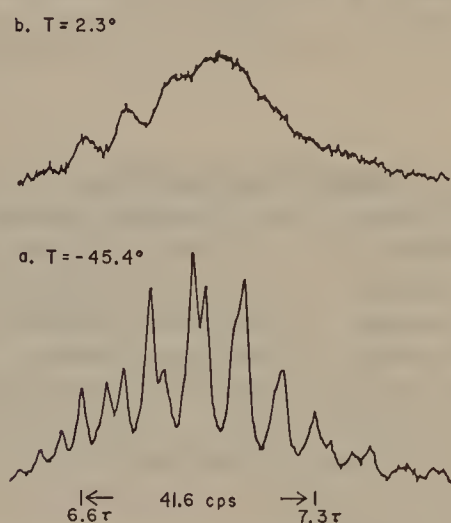
Figure 2. Temperature dependence of methylene resonance in *trans*-bis(diethyl sulfide)dichloroplatinum(II).

The low-temperature nmr spectra of **3** and **4** are too complex to permit complete analyses, but four quartets can be extracted from the center of the methylene sig-

nals; from their relative spacings they can be assigned as the AB part of an ABM$_3$ system. This enabled determination of $\Delta\nu_{AB}$ which was found to be temperature dependent (Figure 4). This linear relationship
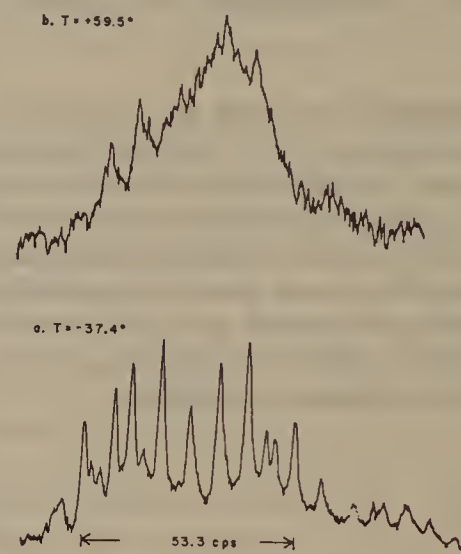
Figure 3. Methylene region in nmr of *cis*-[(Et$_2$S)$_2$PtCl$_2$].

($\Delta\nu$ *vs.* T) observed in the absence of exchange permits the true chemical shift, $\Delta\nu$, to be obtained at the coalescence temperature. For **4**, the least-squares line observed over the temperature range −50 to −15° is

$$\Delta\nu = -0.073T + 16.44 \quad (1)$$
$$\sigma_{slope} = 0.003 \quad \sigma_{intercept} = 0.09$$

For **3**, the least-squares line observed over the temperature range −50 to +20° is

$$\Delta\nu = -0.025T + 30.68 \quad (2)$$
$$\sigma_{slope} = 0.004 \quad \sigma_{intercept} = 0.09$$

The rate constants and free energies of activation for sulfur inversion at the coalescence temperature are listed in Table I.

cis-Bis(methyl benzyl sulfide)dichloroplatinum(II). The methylene region of the nmr spectrum of **5** is not resolved enough for analysis. However, the methyl region is quite suitable for rate determinations (Figure 5). The two 1:4:1 triplets, Figure 5a, are assigned to the *meso* and *dl* isomers which arise from the two asymmetric sulfur atoms in the complex. The peak separa-
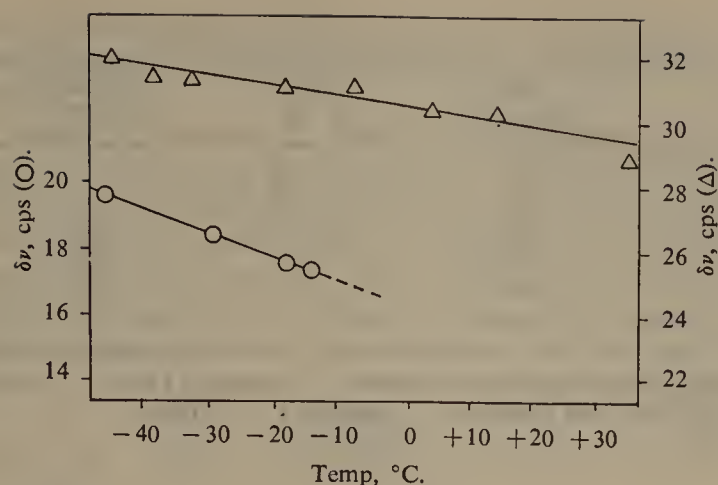
Figure 4. The dependence of chemical shift on temperature in cis-bis(diethyl sulfide)dichloroplatinum(II) (Δ) and trans-bis(diethyl sulfide)dichloroplatinum(II) (O).

tion between the *cis* methyl signals of **5** is linearly dependent upon temperature in the range -90 to $0°$ in methylene chloride, and the least-squares relationship is

$$\Delta\nu = -0.050T + 8.35 \qquad (3)$$

$$\sigma_{\text{slope}} = 0.001 \qquad \sigma_{\text{intercept}} = 0.06$$

Since the two methyl sites appear equally populated, rate equations[9] used previously[3] are applicable. Rate determinations above the coalescence temperature were complicated by the appearance of a new 1:4:1 triplet which was assigned to *trans*-bis(methyl benzyl sulfide)-dichloroplatinum(II) (**6**) and enabled determination of $J_{\text{Pt-S-C-H}}$ in the *trans* isomer. The rate constants and activation parameters are given in Table I. A plot of log k vs. $1/T$ is shown in Figure 6.

Bis(dimethyl sulfide)dichloroplatinum(II) Complexes. The nmr spectrum of our preparation of $[(CH_3)_2S]_2$-$PtCl_2$ consisted of two 1:4:1 triplets in the methyl region. The high-field resonances (17% of spectrum) are centered at -149 cps from TMS with $J_{\text{Pt-S-C-H}} = 41.0$ cps. The low-field set (83% of spectrum) is centered at -156 cps with $J_{\text{Pt-S-C-H}} = 49.5$ cps. On the basis of Pt–H couplings, the latter set is assigned to the *cis* isomer.[8]

Platinum–Proton Coupling Constants. Above the coalescence temperatures it was possible to determine vicinal platinum–proton coupling constants for compounds **1–8**. These couplings and the *cis–trans* ratios are shown in Table II.

Table II. Vicinal Platinum–Proton Coupling Constants in *cis*- and *trans*-Bis(dialkyl sulfide)dichloroplatinum(II) Complexes

	$J_{\text{Pt-S-C-H}}{}^a$		$J_{trans}/$
Sulfide ligand	cis	trans	J_{cis}
$(C_6H_5CH_2)_2S^{b,c}$	43.0	37.0	0.86
$(CH_3CH_2)_2S^{b,d}$	46.4	37.2	0.80
$CH_3SCH_2C_6H_5$	49.7	41.6	0.84
$(CH_3)_2S$	49.5	41.0	0.83

[a] Estimated uncertainty in coupling constants is ±0.5 cps. [b] Coupling constants were measured above the coalescence temperature. Coupling constants given for italic hydrogens. [c] $J_{\text{H-C-H}} = -13.0$ cps. [d] $J_{\text{H-C-C-H}} = 7.4$ cps for both isomers; $J_{\text{H-C-H}} = -12.0$ and -11.6 cps for *cis* and *trans* isomers, respectively.

(9) A. Allerhand, H. S. Gutowsky, J. Jonas, and R. Meinzer, *J. Am. Chem. Soc.*, **88**, 3185 (1966).
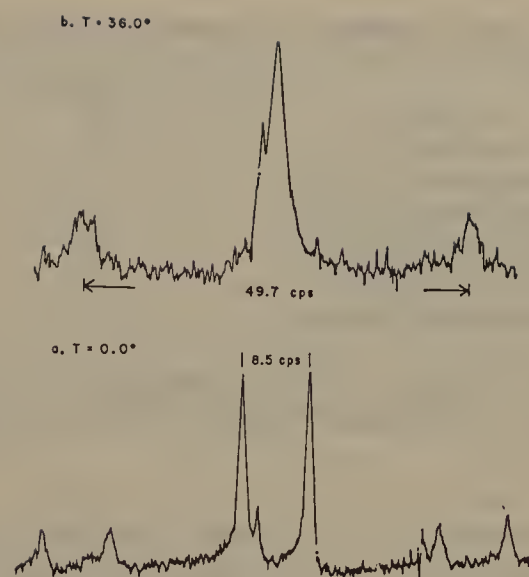
Figure 5. Temperature dependence of methyl region in nmr spectrum of cis-$[(MeSCH_2C_6H_5)_2PtCl_2]$. Solvent is CH_2Cl_2.
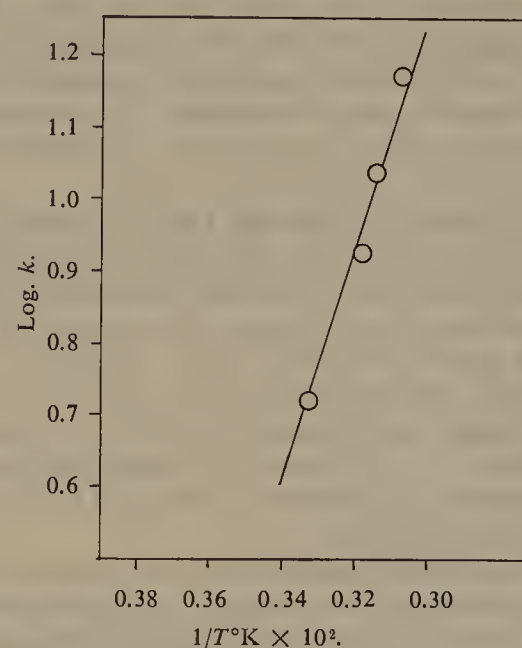
Figure 6. Arrhenius plot for sulfur inversion in *cis*-bis(methyl benzyl sulfide)dichloroplatinum(II).

Two vicinal Pt–H couplings are known below the coalescence temperature. In the *cis* dibenzyl sulfide complex (**1**), $J_{\text{Pt-S-C-H}_A} = 55.7$ cps and $J_{\text{Pt-S-C-H}_B} = 29.3$ cps.[3] In the *cis* methyl benzyl sulfide complexes (*dl* and *meso*), $J_{\text{Pt-S-C-H}_3} = 49.7$ cps for both diastereoisomers.

Discussion

The Inversion Process. The AB nature of the benzylic protons in the pmr spectrum of **1** and the spectral observations of other platinum–sulfide complexes studied are consistent with a nonplanar sulfur configuration.[3] These data supplement some solid-state analyses where the sulfur atom was found to be pyramidal in metal complexes.[10] The facile inversion process is a departure from the behavior of the other tricoordinated sulfur compounds.

(10) (a) C.-I. Branden, *Arkiv Kemi*, **22**, 83 (1964); (b) P. Woodward, L. F. Dahl, E. W. Abel, and B. C. Crosse, *J. Am. Chem. Soc.*, **87**, 5251 (1965).

Table III. Rates of Inversion in Tricoordinated Sulfur Compounds

Compound	Temp, °C	k, sec^{-1}	ΔH^*, kcal/mole	ΔS^*, eu	Rel rate[a] at 25°
$CH_3SO\text{-}p\text{-}C_6H_4CH_3{}^a$	250	6.7×10^{-5}	43	+3	1
$C_6H_5CH_2SO\text{-}p\text{-}C_6H_4CH_3{}^{a,b}$	145	7.3×10^{-5}	43	+24	$10^{4.5}$
$CH_3CH_2S^+(CH_3)C(CH_3)_3{}^c$	50	4×10^{-4}	25^d		10^{13}
$cis\text{-}[(C_6H_5CH_2)_2S]_2PtCl_2{}^e$	25	10	17.4	+3	10^{18}
$cis\text{-}[(CH_3CH_2)_2S]_2PtCl_2{}^e$	60	65	18^d		10^{18}
$trans\text{-}[(CH_3CH_2)_2S]_2PtCl_2{}^e$	1	36	15^d		10^{20}

^{a} In xylene or acetone, ref 12c. ^{b} Evidence found for a homolytic dissociation–recombination mechanism. ^{c} In ethanol, ref 16. ^{d} Calculated from rate constants assuming $\Delta S^* = 3$ eu as in the two cases where ΔS^* has been measured. ^{e} This work; see Table I.

Sulfoxides invert at measurable rates with hydrogen chloride catalysis;[11] however, the mechanism involves a bimolecular chemical reaction where the intermediate is a sulfur dihalide compound with a plane of symmetry and therefore incapable of optical activity.[11b] In the absence of catalysis, vigorous thermal[12] and photolytic[13] conditions are required for inversion. Except in special cases, thermal inversion of sulfoxides appears to proceed through a pyramidal inversion mechanism.[12c] Benzyl p-tolyl sulfoxide is a special case where homolytic dissociation of benzyl radicals appears to be involved in inversion at 135–155°.[12c]

Sulfonium salts are another type of tricoordinated sulfur compound which do not invert readily.[14] Kincaid and Henriques[15] calculated an activation energy of 100 kcal/mole for inversion of a sulfonium sulfur through a planar transition state. However, recent measurements indicate that inversion in t-butylethylmethylsulfonium ion proceeds at 50° with a first-order rate constant > 10^{-4} sec^{-1}.[16] Although activation parameters were not evaluated, ΔH^* must be lower than the theoretical estimates.

The rate constants and activation parameters which have been measured for inversion at pyramidal sulfur are summarized in Table III. The relative rates show that inversion in the sulfide complexes we have studied is immensely faster than in sulfoxides and 10^5–10^7 times faster than in sulfonium salts.

At least three mechanisms for sulfur inversion must be considered: tunneling, inversion through a trigonal planar state, and a dissociation–recombination pathway. A dissociation–recombination pathway for the inversion process in platinum–sulfide complexes is impossible since we observe no loss of Pt–S–C–H coupling above the coalescence temperature.[3]

The height of the potential barrier to inversion in these complexes is not known, so it is difficult to predict the contribution from tunneling. However, related considerations indicate that the contribution from tunneling

should not be large relative to the total height of the barrier.[15, 17]

Considerations of Inversion through a Trigonal Planar State. Nitrogen inversion has been studied in aliphatic amine compounds;[18, 19] the process involves passage through a trigonal planar state (the contribution to inversion from tunneling has not been determined). There appear to be at least five factors influencing the energy required for nitrogen inversion: (1) mass of the atoms directly bonded to nitrogen (for tetramethylaziridine, $E_a = 11.5$ kcal/mole, and for 1-deuteriotetramethylaziridine, $E_a = 14.7$ kcal/mole;[18c] (2) steric effects (large substituents close to nitrogen should increase the inversion rate since steric interactions are decreased in a planar state);[19] (3) electron repulsion (when the atom bonded to nitrogen contains an electron lone pair, e.g., oxygen, electron repulsion will be greater in the planar state, decreasing the inversion rate);[19c] (4) inductive effects (an electronegative substituent will increase the s character of the unshared pair on nitrogen, decreasing the inversion rate);[19c] (5) conjugative effects (double bond character of the type $N^+=X^-$ increases nitrogen inversion since π-orbital overlap is most effective in a planar system).[19d,e] Since there is O→S π bonding in sulfoxides,[20] they should be a reasonable model for the compounds we have studied where there is Pt→S π bonding.[3] Therefore, the important comparisons from Table III concern sulfoxides and cis and trans sulfide complexes.

None of the effects mentioned above appear capable of explaining the 10^{18}–10^{20} rate differences between sulfoxides and sulfide complexes with inversion through a planar state. In fact, a large effect would probably be the mass effect which would predict a slower rate of inversion of the sulfide complexes compared to sulfoxides. We therefore must reject the three mechanisms suggested above for inversion of the sulfide complexes although they have been suggested for sulfoxides;[12]

(11) (a) C. R. Johnson and D. McCants, Jr., *J. Am. Chem. Soc.*, 86, 2935 (1964); (b) K. Mislow, T. Simmons, J. T. Melillo, and A. L. Ternay, Jr., *ibid.*, 86, 1452 (1964); (c) C. R. Johnson and D. McCants, Jr., *ibid.*, 87, 5404 (1965).

(12) (a) H. B. Henbest and S. A. Khan, *Proc. Chem. Soc.*, 56 (1964); (b) K. Mislow, P. Schneider, and A. L. Ternay, Jr., *J. Am. Chem. Soc.*, 86, 2957 (1964); (c) D. R. Rayner, E. G. Miller, P. Bickert, A. J. Gordon, and K. Mislow, *ibid.*, 88, 3138 (1966).

(13) K. Mislow, M. Axelrod, D. R. Rayner, H. Gotthardt, L. M. Coyne, and G. S. Hammond, *ibid.*, 87, 4958 (1965).

(14) M. P. Balfe, J. Kenyon, and J. Phillips, *J. Chem. Soc.*, 2554 (1930).

(15) J. F. Kincaid and F. C. Henriques, Jr., *J. Am. Chem. Soc.*, 62, 1474 (1940).

(16) D. Darwish and G. Tourigny, *ibid.*, 88, 4303 (1966).

(17) (a) G. Herzberg, "Infrared and Raman Spectra," D. Van Nostrand Co., Inc., Princeton, N. J., 1945, p 222; (b) W. Gordy, W. V. Smith, and R. F. Trambarulo, "Microwave Spectroscopy," John Wiley and Sons, Inc., New York, N. Y., 1953, p 127; (c) R. S. Berry, *J. Chem. Phys.*, 32, 933 (1960).

(18) (a) H. S. Gutowsky, *Ann. N. Y. Acad. Sci.*, 70, 786 (1953); (b) W. N. Speckamp, U. K. Pandit, and H. O. Huisman, *Tetrahedron Letters*, 44, 3279 (1964); (c) T. J. Bardos, C. Szantay, and C. K. Navada, *J. Am. Chem. Soc.*, 87, 5797 (1965).

(19) (a) A. T. Bottini and J. D. Roberts, *ibid.*, 80, 5203 (1958); (b) A. Loewenstein, J. F. Neumer, and J. D. Roberts, *ibid.*, 82, 3599 (1960); (c) D. L. Griffith and J. D. Roberts, *ibid.*, 87, 4089 (1965); (d) F. A. L. Anet, R. D. Trepka, and D. J. Cram, *ibid.*, 89, 357 (1967); (e) F. A. L. Anet and J. M. Osyany, *ibid.*, 89, 352 (1967).

(20) P. Haake, W. B. Miller, and D. A. Tyssee, *ibid.*, 86, 3577 (1964).

a benzyl sulfoxide appears to invert by a dissociative mechanism and most sulfoxides appear to invert *via* a planar state.

Inversion through a Partially Dissociated State. The multiple bonding possibilities available in platinum(II) complexes lead us to suggest an inversion mechanism in which sulfur retains its distorted tetrahedral configuration and some bonding to platinum persists through the inversion process. This process is depicted below.

9
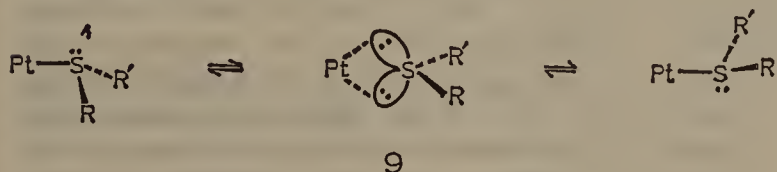
The configuration **9**, midway in the inversion process, could be an intermediate or a transition state, but a reasonable hypothesis is that there is bonding to both sulfur unshared pairs so that the platinum atom has a distorted pentacoordinate configuration in **9**.[21] The inversion process then is really an internal displacement of one sulfide pair by another sulfide pair in a rearrangement mechanism similar to that suggested for displacement on platinum(II).[22] This proposal is con-

sistent with the retention of Pt–S–C–H coupling above the coalescence temperature, since bond weakening and bond strengthening are involved but there is never opportunity for dissociation of the sulfide ligand.

In **9**, R, R′, Pt, and S are coplanar, but the important difference between this proposal and the suggested mechanism of inversion at nitrogen and at sulfoxide sulfur is that the configuration of sulfur is tetrahedral, not trigonal, in **9**.[23] Also, this proposal would mean there is an internal displacement at platinum rather than true inversion at sulfur in these complexes.

Platinum–Proton Coupling Constants. The average ratio of J_{trans}/J_{cis} is 0.83 (Table II). Three explanations are possible based on coupling through σ bonds, π bonds, and space. Coupling through space is rare.[24] The amount of s character in the π bonds must be small. Therefore, the most reasonable explanation for this ratio is the increased strength of the σ Pt–S bonds in the *cis* isomers due to increased Pt→S π bonding which makes the *cis* sulfurs better ligands than the *trans* sulfurs.[8,25]

Acknowledgment. We are particularly indebted to the late Dr. A. J. R. Bourn and to Professor F. A. L. Anet for valuable discussions and help with the instrumentation.

(21) (a) E. L. Muetterties and R. A. Schunn, *Quart. Rev.* (London), **20**, 245 (1966); (b) L. M. Venanzi, *Angew. Chem. Intern. Ed. Engl.*, **3**, 453 (1964).

(22) (a) P. Haake, *Proc. Chem. Soc.*, 278 (1962); (b) C. H. Langford and H. B. Gray, "Ligand Substitution Processes," W. A. Benjamin, Inc., New York, N. Y., 1965.

(23) A similar proposal has been advanced for sulfide–borane complexes where the state corresponding to **9** should be a transition state: T. D. Coyle and F. G. A. Stone, *J. Am. Chem. Soc.*, **83**, 4138 (1961).

(24) F. A. L. Anet, A. J. R. Bourn, P. Carter, and S. Winstein, *ibid.*, **87**, 5249 (1965).

(25) P. S. Braterman, *Inorg. Chem.*, **5**, 1085 (1966).

Olefin Coordination Compounds of Rhodium. V. The Relative Stabilities and Rates of Exchange of Olefin Complexes of Rhodium(I)

Richard Cramer

Contribution No. 1246 from the Central Research Department, Experimental Station, E. I. du Pont de Nemours and Company, Wilmington, Delaware. Received March 17, 1967

Abstract: The stabilities of a number of olefin complexes of rhodium(I) have been compared. Alkyl substituents on olefin carbons destabilize rhodium(I) complexes much more than the corresponding silver compounds. Conversely, coordination is enhanced by electronegative substituents, and this is attributed to a stronger π or back-bond. Since C_2F_4 (which coordinates very strongly) displaces ethylene from rhodium(I) much more slowly than do propene or butenes (which coordinate weakly), it is inferred that formation of a π bond plays a minor role in the development of the transition state for nucleophilic olefin exchange.

The bond uniting olefins and transition metals is currently described[1] as comprising (1) a σ bond formed by overlap of the filled π orbital of the olefin with an empty σ-type orbital of the metal atom and (2) a π-type "back-bond" from overlap of a filled, metal d_{xy} or

other $d\pi$–$p\pi$ hybrid orbital with the antibonding π orbital of the olefin. It is expected that the strength of both the σ bond and π "back-bond" are affected by olefin structure. For example, an electronegative olefin substituent, by reducing the electron density of the olefin, would weaken the σ bond and strengthen the π bond. Depending upon the relative contributions of each, the

(1) M. J. S. Dewar, *Bull. Soc. Chim. France*, **18**, C79 (1951); J. Chatt and L. A. Duncanson, *J. Chem. Soc.*, 2939 (1953).
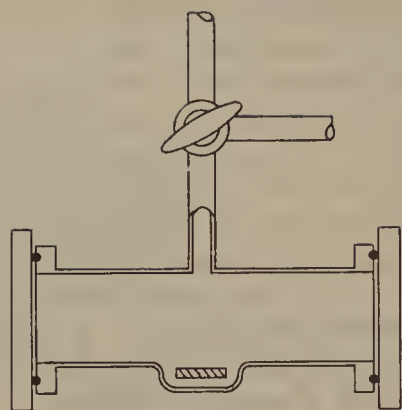
Figure 1. Reaction cell for spectrophotometric analysis.

complex of a substituted ethylene might be more or less stable than that of ethylene itself.

Considerable attention has been given to the effect of structure on the stability of hydrocarbon complexes, particularly of silver;[2] much less information is available on silver compounds of functionally substituted olefins.[3a] Some quantitative results are also reported for copper(I) compounds of alkyl- and functionally substituted olefins[3] and for platinum(II) complexes of olefins of the type $RRC=CR(CH_2)_nL^+R_3^4$ (L = N, P, As; $n = 1$ or 2; R = H or alkyl, not necessarily identical).

The results may be summarized as follows. (1) Enthalpy increments (determined through the change with temperature of the vapor pressure of the unsaturated ligand over the appropriate solid complex) indicate that alkylated olefins form stronger bonds to silver(I)[2b] or copper(I)[3c] than does ethylene. Also, copper is more strongly bonded to acrylonitrile[3d] ($\Delta H_f = -14.9$ kcal mole^{-1}) and acrolein[3e] ($\Delta H_f = -11.8$ kcal mole^{-1}) than to propylene[3c] ($\Delta H_f = -11.0$ kcal mole^{-1}) or ethylene[3c] ($\Delta H_f = -11.0$ kcal mole^{-1}). (2) In spite of the enthalpy values, $CuCl \cdot C_3H_6$ dissociates more completely than $CuCl \cdot C_2H_4$ over a wide temperature range. The vapor pressures (in atmospheres) developed at 0° by copper(I) compounds increase in the following order: $CuCl \cdot CH_2=CHCN$ (0.014, extrapolated)[3d] < $CuCl \cdot CH_2=CHCHO$ (0.038)[3e] < $CuCl \cdot C_2H_4$ (1.95)[3b] < $CuCl \cdot C_3H_6$ (2.6, extrapolated).[3b] In solution, propylene–silver complex dissociates more completely than the ethylene compound.[2a] (3) Stabilities of platinum complexes[4a,d] increase with structure modifications which reduce electron density at the olefin bond.

In addition to these quantitative results, a special stabilization of olefin complexes by electronegative substituents[5] is indicated by the facile synthesis and relatively high stability of numerous compounds.

(2) (a) M. A. Muhs and F. T. Weiss, J. Am. Chem. Soc., 84, 4697 (1962), and references cited there; (b) H. W. Quinn and D. N. Glew, Can. J. Chem., 40, 1103 (1962).

(3) (a) J. Chatt in "Cationic Polymerization and Related Complexes," P. H. Plesch, Ed., W. Heffer and Sons, Ltd., Cambridge, England, 1953, pp 44–47; (b) E. R. Gilliland, J. E. Seebold, J. R. Fitz-Hugh, and P. S. Morgan, J. Am. Chem. Soc., 61, 1960 (1939); (c) E. R. Gilliland, H. L. Bliss, and C. E. Kip, ibid., 63, 2088 (1941); (d) G. N. Schrauzer, Chem. Ber., 94, 1891 (1961); (c) S. Kawaguchi and T. Ogura, Inorg. Chem., 5, 844 (1966).

(4) (a) R. G. Denning, F. R. Hartley, and L. M. Venanzi, J. Chem. Soc., Sect. A, 324 (1967); (b) ibid., 328 (1967); (c) F. R. Hartley and L. M. Venanzi, ibid., 333 (1967); (d) R. G. Denning and L. M. Venanzi, ibid., 336 (1967).

(5) Cf. G. N. Schrauzer, Chem. Ber., 94, 642 (1961).

These include complexes of manganese,[6a] iron,[6b] nickel,[6c,d] copper,[6e] rhodium,[6b,g] and platinum[6h] with olefins substituted by carboxyl,[6b,d,f,h] cyano,[6a–c,e,f,h] or halogen.[6g,h]

The properties of 2,4-pentanedionatobis(ethylene)-rhodium(I), acacRh(C$_2$H$_4$)$_2$, suggest it may be used conveniently to measure the effect of olefin substituents on the stability of complexes with rhodium(I). This compound is thermodynamically stable; thus, the extent of dissociation of ethylene in ethylene glycol solution is less than 0.1% at 80°. However the coordinated ethylene is kinetically labile; in the presence of free ethylene at −50° the half-life of coordinated ethylene is less than 10^{-2} sec. When solutions of the complex are treated with an olefin, ethylene is displaced to some extent according to eq 1. In an open reactor an excess

$$acacRh(C_2H_4)_2 + olefin \xrightleftharpoons{} acacRh(C_2H_4)(olefin) + C_2H_4 \quad (1)$$
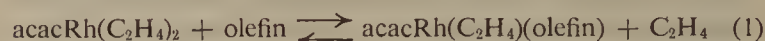
of olefin will generally replace both ethylene ligands to give acacRh(olefin)$_2$, but measurements may be confined to concentrations appropriate to eq 1. Its equilibrium constant reflects the strength of the coordination bond between rhodium(I) and the added olefin as compared to the rhodium–ethylene bond.

The extent and rate of ethylene displacement from acacRh(C$_2$H$_4$)$_2$ was measured by infrared spectrophotometric analysis of the gas over the reaction solution using the cell shown in Figure 1. A dilation of the cell held a solution of acacRh(C$_2$H$_4$)$_2$, which was stirred by a polytetrafluoroethylene-covered magnet. Gaseous olefins were used in most experiments, and these were introduced through a three-way stopcock. The cell-holder was a polyethylene dish in which the cell dilation was immersed in water at a controlled temperature. The technique is very convenient and moderately precise.

Equilibrium was generally attained within a few minutes, but with some highly substituted olefins or in dilute solutions reaction was slow enough to obtain kinetic data.

Experimental Section

A Perkin-Elmer Model 237 spectrophotometer was used at slow scan speed. The general procedure was to charge the cell with a measured amount of olefin and acacRh(C$_2$H$_4$)$_2$ in toluene solution. The quantity of ethylene released was measured through the absorptivity of the gas phase at 10.5 μ, and this was supplemented in some experiments by a similar evaluation of noncoordinated added olefin based on a characteristic absorption. From these data and estimates of the solubilities of ethylene and the other olefin in the reaction medium, approximate equilibrium constants could be calculated.

The detailed procedures depended upon the nature of the olefin which was employed to displace ethylene. Typical examples follow.

Displacement by Vinyl Chloride. A solution of 0.0129 g (0.050 mmole) of acacRh(C$_2$H$_4$)$_2$ in 2.00 ml of toluene was pipetted into the cell and frozen by immersing the dilation in liquid nitrogen. The

(6) (a) M. L. Zeigler and R. K. Sheline, Inorg. Chem., 4, 1230 (1965); (b) E. Weiss, K. Stark, J. E. Lancaster, and H. D. Murdoch, Helv. Chim. Acta, 46, 288 (1963); (c) G. N. Schrauzer, J. Am. Chem. Soc., 81, 5310 (1959); (d) E. Weiss and K. Stark, Z. Naturforsch., 20b, 490 (1965); (e) G. N. Schrauzer and S. Eichler, Chem. Ber., 95, 260 (1962); (f) L. Porri and A. Lionetti, J. Organometal. Chem. (Amsterdam), 6, 422 (1966); (g) R. Cramer and G. Parshall, J. Am. Chem. Soc., 87, 1392 (1965); (h) W. J. Bland and R. D. Kemmitt, Nature, 211, 963 (1966).

cell windows were positioned; the cell was evacuated, placed in the holder containing water at 25 ± 0.2°, and pressured with nitrogen to 100 mm. Vinyl chloride was introduced in increments by hypodermic syringe through a septum attached to one of the arms of the cell stopcock. After each addition the solution was stirred and the spectrum recorded after equilibration (less than 10 min). The amount of ethylene liberated was estimated by comparison of the absorbance at 10.5 μ with an empirical curve relating optical density to ethylene charge in this cell under the conditions of the experiment. Assuming eq 1, the amounts of C_2H_4, C_2H_3Cl, acacRh$(C_2H_4)_2$, and acacRh$(C_2H_4)(C_2H_3Cl)$ in the cell could be calculated. The results are shown in Table I.

Table I. Equilibrium: $C_2H_3Cl + acacRh(C_2H_4)_2 \overset{25°}{\underset{}{\rightleftharpoons}}$
$C_2H_4 + acacRh(C_2H_4)(C_2H_3Cl)$

Added C_2H_3Cl, ml	Released C_2H_4, mmole	Noncoord C_2H_3Cl, mmole	acacRh-$(C_2H_4)_2$, mmole	K_E
0.25	0.0088	0.0012	0.0412	0.187
0.50	0.0156	0.0044	0.0344	0.197
1.00	0.0224	0.0176	0.0276	0.126
1.50	0.0300	0.0300	0.0200	0.182
2.00	0.0336	0.0464	0.0164	0.181
2.50	0.0344	0.0656	0.0156	0.142
			Average	0.170 ± 0.019[a]

[a] The probable error is calculated as 0.674 × sample standard deviation; see E. B. Wilson, Jr., "An Introduction to Scientific Research," McGraw-Hill Book Co., Inc., New York, N. Y., 1952, p 255.

Ethylene and vinyl chloride are distributed between the gas and liquid phases in proportions which depend upon their solubility in toluene. Thus at 25° and an ethylene pressure of 1 atm, 3.02 ml of ethylene dissolves in 1 ml of toluene.[7] Since the volume of the cell was 83.0 ml and it contained 2.00 ml of toluene, about 2 × 3.02/[2 × 3.02 + (83.0 − 2.00)] or 0.0694 of the ethylene in the cell was dissolved. The solubility of vinyl chloride is estimated (see following paragraph) to be 52.9 ml/ml of toluene. A similar calculation indicates 0.567 of the vinyl chloride was dissolved. Equilibrium constants were calculated using the formula

$$K_E = \frac{[acacRh(C_2H_4)(C_2H_3Cl)][C_2H_4]f_{C_2H_4}}{[acacRh(C_2H_4)_2][C_2H_3Cl]f_{C_2H_3Cl}}$$

where concentrations are in millimoles and $f_{C_2H_4}$ = fraction of C_2H_4 in solution. It is assumed that mmole of acacRh(C_2H_4)-(C_2H_3Cl) = mmole of C_2H_4.

Since solubilities in toluene have not been reported for most of the olefins used here, it was generally assumed that these all give ideal solutions and that the solubilities of the gaseous olefins are inversely proportional to their saturation pressures. These saturation pressures were calculated by interpolation of data from various sources and are given along with the estimated gas solubilities in Table II.

Displacement by Tetrafluoroethylene. Unlike most olefins listed in Tables III and IV, tetrafluoroethylene displaces ethylene from acacRh$(C_2H_4)_2$ so slowly that the rate may be followed conveniently by observing the change in absorbance at 10.5 μ. The kinetics (reaction of 0.5 mmole each of acacRh$(C_2H_4)_2$ and C_2F_4 in 2.00 ml of toluene) correspond to a second-order reaction since a plot of OD/(OD$_\infty$ − OD) against time is linear[8] (Figure 2).

For tetrafluoroethylene, the equilibrium in eq 1 lies far to the right, so it is experimentally advantageous in determining the equilibrium constant to measure unreacted C_2F_4 (using the absorption

(7) Calculated from data of D. B. Todd and J. C. Elgin, *A.I.Ch.E. J.*, **1**, 20 (1955).
(8) A. A. Frost and R. G. Pearson, "Kinetics and Mechanism," 2nd ed, John Wiley and Sons, Inc., New York, N. Y., 1961, pp 28–30, 37–38.
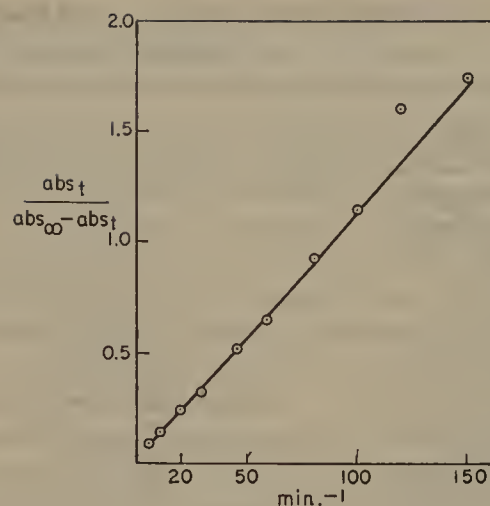
Figure 2. Rate of displacement of C_2H_4 from acacRh$(C_2H_4)_2$ by C_2F_4.

at 8.4 μ) rather than liberated C_2H_4. Since it was expected that tetrafluoroethylene might deviate widely from ideal solubility, measured solubilities of ethylene[7] and tetrafluoroethylene were employed for calculations. The values used were: ethylene, 4.35 (0°), 3.02 (25°); tetrafluoroethylene, 2.00 (0°), 1.43 (25°) ml of gas/ml of solvent (1 atm gas pressure).

Displacement by Styrene. This experiment is typical for liquid olefins. The dilation of the cell was charged with 0.100 mmole of styrene in 2.0 ml of toluene. The solution was frozen with liquid nitrogen, and 0.050 mmole of solid acacRh$(C_2H_4)_2$ was added. The cell was closed, evacuated, warmed to 25.0 ± 0.2°, and pressured to 100 mm with nitrogen. The amount of released ethylene,

Table II. Saturation Pressures and Solubilities of Olefins

	0°		25°	
	Satn pressure, mm	Solubility, ml of gas/ml of toluene	Satn pressure, mm	Solubility, ml of gas/ml of toluene
Ethylene[b]	30,500	(4.35)	51,500[f]	(3.02)
Propylene[b]	4,400	30.2	8,700	17.9
1-Butene[a,b]	964	138	2,200	70.6
cis-2-Butene[a]	658	202	1,600	97.2
trans-2-Butene[a]	733	181	1,780	87.5
Isobutylene[a]	988	134	2,300	67.6
Vinyl fluoride[c]	11,000	12.1	21,000	7.40
Vinyl chloride[d]	1,290	103	2,940	52.9
cis-1,2-Difluoroethylene[e]	2,137	62.1	4,930	31.6
trans-1,2-Difluoroethylene[e]	6,210	21.4	12.900	12.1

[a] J. Timmermans, "Physico-Chemical Constants of Pure Organic Compounds," Elsevier Publishing Co., Inc., New York, N. Y., 1950, pp 115–123. [b] Footnote a, Vol. II, 1965, pp 61–66. [c] E. I. du Pont de Nemours and Co., Inc., Organic Chemicals Department, New Products Report -201-F, Sept 11, 1959. [d] R. A. McDonald, S. A. Shrader, and D. R. Stull, *J. Chem. Eng. Data*, **4**, 311 (1959). [e] 1,2-Difluoroethylene was prepared by dechlorination of CHFCl-CHFCl (W. S. Durrell, G. Westmoreland, and M. G. Moshonas, *J. Polymer Sci.*, A3, 2975 (1965)), and the isomers were separated by glc. The vapor pressure of cis-1,2-difluoroethylene was measured from −36 to +10° and over this range it corresponds to the equation log P = 7.635 − 1.175T^{-1} × 10^3 ± 0.003. The tabulated pressure at 0° is the measured value while the pressure at 25° was obtained by extrapolation. The vapor pressure of trans-1,2-difluoroethylene was measured between −53 and −26° and over that range corresponds to log P = 7.564 − 1.029T^{-1} × 10^3 ± 0.006. The tabulated pressures were obtained by extrapolation. [f] This value for the "saturation pressure" of ethylene at 25° was obtained by extrapolating the log vapor pressure *vs.* 1/T plot beyond the critical temperature of ethylene.

Table III. Equilibrium Constants, Enthalpies, and Entropies

$$\text{olefin} + \text{acacRh(C}_2\text{H}_4)_2 \underset{\longleftarrow}{\overset{\longrightarrow}{\rightleftharpoons}} \text{acacRh(C}_2\text{H}_4)(\text{olefin}) + \text{C}_2\text{H}_4$$
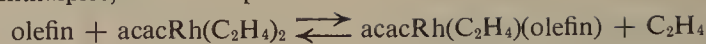
Olefin	$K_E \times 10^3$ (25°)	$K_E \times 10^3$ (0°)	ΔH, kcal mole^{-1}	ΔS, eu
$CH_2=CHCH_3$	78 ± 7	63 ± 8	1.4 ± 0.9	-0.5 ± 0.5
$CH_2=CHC_2H_5$	92 ± 18	79 ± 12	1.0 ± 1.4	-1.7 ± 5.0
cis-C_4H_8	4.1 ± 0.3	3.1 ± 0.3	1.8 ± 0.8	-4.9 ± 3.0
trans-C_4H_8	2.0 ± 0.3	1.5 ± 0.1	1.9 ± 0.7	-6.1 ± 2.6
i-C_4H_8	0.35 ± 0.02	0.19 ± 0.02	3.9 ± 0.7	-2.6 ± 2.5
$CH_2=CHCl$	170 ± 19	150 ± 10	0.8 ± 0.8	-0.8 ± 2.9
$CH_2=CHF$	320 ± 22	410 ± 70	-1.6 ± 1.1	-7.5 ± 3.8
trans-$CHF=CHF$	1240 ± 360	1320 ± 410		
cis-$CHF=CHF$	1590 ± 330	2080 ± 460		
$CH_2=CF_2{}^a$	100 ± 10			
$CH_2=CHOCH_3{}^b$	18 ± 2			

[a] Based on a measured value for the solubility of $CH_2=CF_2$ of 2.46 ml of $CH_2=CF_2$/ml of toluene.   [b] Based on a measured valued for the solubility of $CH_2=CHOCH_3$ of 167 ml of $CH_2=CHOCH_3$/ml of toluene.

measured as described earlier, was found to be 0.036 mmole. The vapor pressure of styrene at 25° is about 7 mm, and if it is assumed that the partial pressure is proportional to the mole fraction (about 0.005), virtually all the unreacted styrene is in solution. Since, as calculated earlier, 0.0694 of the ethylene is in solution, $K_E = (0.036)(0.036 \times 0.069)/(0.014 \times 0.064) = 0.100$.

Synthesis of acacRh($CH_2=CHCl$)$_2$. A flask was charged with 0.50 g of acacRh(C_2H_4)$_2$, evacuated, and chilled to $-25°$. Vinyl chloride (about 10 ml) was condensed in the flask which was then warmed slightly to distil unreacted vinyl chloride within 20 min. The residue was again treated in similar fashion with about 10 ml of vinyl chloride to get a yellow oil. This crystallized when washed with isobutane at $-50°$. The product (0.48 g, 76% yield) was recovered (by removing isobutane at $-50°$ under nitrogen through a filter stick) and dried at 1 mm (20°) for 0.5 hr. It melted at 42–43°. *Anal.* Calcd for $C_9H_{13}O_2RhCl_2$: C, 33.06; H, 4.01; Cl, 21.69. Found: C, 32.38; H, 4.21; Cl, 21.11. A sample (KBr wafer) absorbed at 3000 (m), 2930 (w), 1620 (?, sh), 1570 (s), 1458 (sh), 1428 (w), 1378 (s), 1309 (m), 1274 (m), 1230 (w), 1197 (w), 1023 (m), 954 (w), 936 (w), 922 (sh), 782 (m), and 677 (s) cm^{-1}.

The nmr spectrum (in d_6-acetone) has sharp absorptions corresponding to a 2,4-pentanedionato group (-4.99 and -1.53 ppm) and two broad absorptions attributed to vinyl chloride. One is centered at -4.50 ppm and the other at -3.05 ppm (integrated ratio 1/2.4).

Synthesis of acacRh(C_3H_6)$_2$. A 0.5-g sample of acacRh(C_2H_4)$_2$ was treated three times with about 20 ml of liquid CH_3Cl and 10 ml of liquid C_3H_6 as described earlier for synthesis of the vinyl chloride complex. (Methyl chloride was used to raise the reflux temperature of the reaction mixture.) The product was a light brown solid melting at 40°. The yield was 0.4 g (73%). *Anal.* Calcd for $C_{11}H_{19}O_2Rh$: C, 46.16; H, 6.69. Found: C, 45.11; H, 6.56. Reaction with aqueous NaCN released a gas identified as propene by its infrared spectrum. Infrared (KBr wafer) absorption was found at 3000 (m), 2930 (sh), 1630 (sh), 1560 (s), 1520 (s), 1423 (sh), 1388 (s), 1272 (m), 1236 (w), 1203 (w), 1056 (m), 987 (w), and 938 (m) cm^{-1}. The nmr spectrum is described in the following section.

Results

Equilibria. Equilibrium constants for eq 1 corresponding to a variety of olefins are given in Tables III and IV. The values in Table III are the means of 6 to 15 observations covering a 6- to 20-fold variation of initial olefin concentration. The listed probable error is based on the range of values found for K and generally amounts to about 10% of the mean. Further uncertain error is introduced by the use of the ratio of olefin vapor pressures for gas solubility ratios. For the few olefins whose solubilities are recorded (ethylene,

propylene, isobutylene) the difference between the ratio of their solubilities and the corresponding ratio of gas vapor pressures is as large as 20% of the solubility ratio. The equilibrium constants in Table IV are based on at least four observations and are believed to have about the same accuracy as those in Table III.

Table IV. Equilibrium Constants[a]

$$\text{olefin} + \text{acacRh(C}_2\text{H}_4)_2 \underset{\longleftarrow}{\overset{\longrightarrow}{\rightleftharpoons}} \text{acacRh(C}_2\text{H}_4)(\text{olefin}) + \text{C}_2\text{H}_4$$
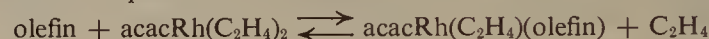
Olefin	K_E (25°)	Olefin	K_E (25°)
$CHF=CF_2$	88	$CH_2=CHC_6H_5$	0.08
$CF_2=CF_2$	59	$CH_2=CHCN$	>50
$CH_2=CCl_2$	No reaction	$CH_2=CHN(CF_3)_2$	0.1
cis-$CHCl=CHCl$	Ca. 0.07	CO	>100
$CCl_2=CCl_2$	No reaction		

[a] Based on the following solubilities (ml of gas/ml of toluene at 25°): C_2H_4 (3.02), $CHF=CF_2$ (4.31), and $CF_2=CF_2$ (1.43). Other olefins are assumed to be concentrated in the liquid phase.

Also included in Table III are calculated values for the enthalpy and entropy change accompanying olefin exchange. Although the probable error is large, these properties appear to be a reasonable basis for qualitative discussion.

The equilibrium constants listed in Table III show that increasing substitution of hydrogen by methyl groups reduces the stability of olefin complexes of rhodium(I). Similar results have been obtained with silver[2,3a,9] and copper(I)[3] compounds. On the other hand, substitution by fluorine increases complex stability. Thus, although the vinyl fluoride complex is less stable than acacRh(C_2H_4)$_2$ ($K = 0.32$), the 1,2-difluoroethylene compounds are about as stable as acacRh(C_2H_4)$_2$, and the trifluoroethylene complex (Table IV) is much more stable.

Stability is also affected by the position of substitution. Complexes of disubstituted ethylene are less stable if the substituents are at the same carbon. Thus, the isobutylene complex ($K = 0.00035$) is less stable than

(9) R. J. Cvetanović, F. J. Duncan, W. E. Falconer, and R. S. Irwin, *J. Am. Chem. Soc.*, **87**, 1827 (1965).

the complexes of cis-2-butene ($K = 0.0041$) or trans-2-butene ($K = 0.0020$). Similarly, complexes of 1,1-difluoro- or 1,1-dichloroethylene are less stable than those of the corresponding 1,2-dihaloethylenes.

The enthalpy increments listed in Table III indicate that displacement of ethylene by propene or a butene is endothermic, but reaction with vinyl fluoride is slightly exothermic. Entropy decreases in all ethylene displacements. (Enthalpy and entropy increments were not calculated for 1,2-difluoroethylenes because the probable error in the equilibrium constants was prohibitively large, possibly as a consequence of partial displacement of the second ethylene ligand.)

Kinetics. Displacement of C_2H_4 in acacRh(C_2H_4)$_2$ by C_2F_4 or C_2F_3H is relatively slow, and only one ethylene ligand is lost. The reaction, which was followed by measuring the rate of release of C_2H_4, has the kinetics of a second-order reaction of the polyfluoroolefin and acacRh(C_2H_4)$_2$. Plots of absorbance$_t$/(absorbance$_\infty$ − absorbance$_t$) against time[8] for reaction with C_2F_4 at 0 and 25° are linear, and the quotient of the slopes when adjusted for the solubility of C_2F_4 in toluene at the two temperatures corresponds to an Arrhenius activation energy of 12 kcal.

If it is assumed that the ratio of solubilities of C_2F_3H in toluene at 0 and 25° is the same as for C_2F_4 at these temperatures, then displacement of ethylene from acacRh(C_2H_4)$_2$ by C_2F_3H has an activation energy of 8 kcal.

Nmr Spectrum of acacRh(CH$_2$=CHCH$_3$)$_2$. Another Route to Relative Stabilities of Olefin Complexes. The nmr spectrum of a solution of acacRh(C_2H_4)$_2$ at 25° exhibits coordinated ethylene as a single sharp absorption.[10] Failure of ethylene protons to be resolved may be attributed to rapid intramolecular exchange, since it has been estimated that the average half-life of coordinated ethylene in acacRh(C_2H_4)$_2$ is less than 10^{-4} sec. When ethylene is added to the test solution, exchange of free and coordinated ethylene is so fast that the spectrum has a single ethylene absorption, broadened and displaced from −2.96 toward −5.3 ppm, the nmr resonance frequency for C_2H_4, to an extent which depends on the amount of free ethylene in the sample.[11]

The nmr spectrum of a CDCl$_3$ solution of acacRh-(CH$_2$=CHCH$_3$)$_2$ has four areas of absorption: (a and b) sharp peaks at −5.32 and −1.99 ppm assigned to protons on the central and terminal carbon atoms, respectively, of coordinated acetylacetonyl; (c) a doublet (split 5 cps) centered at −1.57 ppm attributed to methyl protons of coordinated propylene; and (d) a smeared, irregular quadruplet between −2.65 and −3.40 ppm corresponding to olefinic protons of coordinated propylene. When propylene is added to the solution, the fine structure of the spectrum of uncoordinated propylene is barely changed and nmr absorptions of free and coordinated propylene are clearly distinguishable. Since absorptions of methyl protons of free and coordinated propylene are separated by 14 cps, the half-life of coordinated propylene is estimated[12] to be longer than 0.1 sec.

(10) R. Cramer, *J. Am. Chem. Soc.*, **86**, 217 (1964).
(11) Rapid rotation of coordinated ethylene in acacRh(C_2H_4)$_2$ with the coordination bond as axis would lead to a single absorption for coordinated ethylene in solutions of acacRh(C_2H_4)$_2$.[10] However, it would not account for the effect of added ethylene on the spectrum.
(12) J. A. Pople, W. G. Schneider, and H. J. Bernstein, "High Resolution Nuclear Magnetic Resonance," McGraw-Hill Book Co., Inc., New York, N. Y., 1959, p 223.

When propylene is added to a solution of acacRh-(C_2H_4)$_2$, a part of the ethylene is displaced according to eq 1, and the nmr absorption corresponding to ethylene shifts downfield (as a consequence of exchange of coordinated and displaced ethylene) by an amount which depends on the concentration of displaced ethylene. The concentration of displaced ethylene can be estimated by reference to spectra of solutions containing acacRh(C_2H_4)$_2$ and varying amounts of ethylene. Methyl protons of coordinated acetylacetonyl provide a convenient internal standard for measuring the shift of ethylene proton absorption.

Calculations based on experiments with solutions of 0.10 g of acacRh(C_2H_4)$_2$ and 1.5, 5.0, 10.0, or 25.0 ml of gaseous propylene in 1.0 ml of CDCl$_3$ gave a value for K_E of 0.07 ± 0.01, agreeing with that listed for propylene in Table III.

Discussion

Equilibria. The increased stability of complexes of highly fluorinated olefins (Table III) and parallel results with other polar olefins (Tables III and IV) apparently reflect stabilization by negative substituents superimposed on steric destabilization. Destabilization by electropositive groups is less obvious but nevertheless demonstrable. Propylene is less strongly bonded than ethylene ($K = 0.078$), and a similar trend in silver–olefin complexes has generally been attributed to steric hindrance. However, if data concerning coordination of olefins by silver(I) are put into the form of eq 1, and compared with the corresponding reactions of rhodium(I), it is found that the effect of an alkyl substituent is about ten times as large for rhodium(I) complexes as for the corresponding silver compounds. Thus, substitution of olefinic hydrogen by CH$_3$ reduces the stability of olefin–rhodium complexes by a factor of about 0.03 to 0.08 (column 5, Table V), as compared with approximately 0.2 to 0.5 for silver compounds (column 4, Table V). Consequently, it is proposed that steric hindrance, which accounts for behavior of silver compounds, is augmented by electrical effects in hydrocarbon–rhodium complexes.

Table V. Equilibrium Constants, Enthalpies, and Entropies
$$C_2H_4 \cdot ANgO_3 + \text{olefin} \rightleftharpoons \text{olefin} \cdot AgNO_3 + C_2H_4{}^a$$

Olefin	ΔH, kcal mole^{-1}	ΔS, eu	K_E (25°)	K_E (25°)– Rh^b
CH$_2$=CHCH$_3$	−0.1	−1.5	0.43	0.078
CH$_2$=CHC$_2$H$_5$	−0.3	−2.0	0.50	0.092
cis-C$_4$H$_8$	−0.1	−2.2	0.28	0.0041
trans-C$_4$H$_8$	0.6	−1.7	0.091	0.0020

^{a} Calculated from data of ref 9. ^{b} Comparable rhodium complex, from Table III.

Accordingly, electronegative groups strengthen and electropositive groups weaken coordination of olefins to rhodium(I). Since this is the manner in which the π-bond part of the olefin coordination bond is expected to respond to these substituents, it is concluded that the

electrical effect acts principally through the π bond. This might occur either because the π bond is the stronger bond or because it is more susceptible to inductive effects.[13]

If the enthalpy data of Table III are accepted as significant, they can be interpreted as tending to reinforce the proposed importance of the π bond in electronic effects.[14] Displacements of ethylene by alkylated olefins have a positive enthalpy increment because a weaker coordination bond is formed through a combination of steric and electronic factors.

Conversely, in displacement of ethylene by vinyl fluoride enthalpy decreases because of stronger π bonding. The entropy increment is apparently large enough to overcome a negative enthalpy change giving a positive free-energy change for displacement of ethylene by vinyl fluoride.

In accounting for the relative stabilities of silver(I)–olefin complexes most authors,[2a,3a,15] although recognizing the possible importance of electronic factors, have been concerned with steric effects. However, the greater stability of 3-methylcyclopentene as compared with 4-methylcyclopentene was attributed to electronic effects,[16] and this is supported by molecular orbital

calculations[17] which indicate that the increased stability of 3-methylcyclopentene complex is due to the higher donor power of the double bond leading to a stronger σ bond.

Quinn and co-workers,[2b,13a] in precise measurements involving solid olefin complexes of $AgBF_4$ and $AgClO_4$, have demonstrated a progressive *enthalpy change favoring coordination as ethylene hydrogen is replaced by methyl*. This is in contrast to results reported here for rhodium complexes. They found that the amount of perturbation of the olefin double-bond stretch frequency as a consequence of complex formation ($\nu_{uncomplexed} - \nu_{complexed}$) was linearly related to the olefin ionization potential (equivalent to olefin basicity) and to the enthalpy change accompanying complex formation. These results indicate that in formation of silver complexes, olefin substituents affect the σ bond primarily.

Kinetics. It has been estimated that the half-life of coordinated ethylene in $acacRh(C_2H_4)_2$ is less than 10^{-4} sec at $25°$.[10,18] Although displacement of ethylene by C_2F_4 is thermodynamically favored ($K = 59$), the rate is less than 10^{-6} that of ethylene exchange. This behavior conforms with a mechanism in which the rate-determining step is the nucleophilic addition of the olefin to a d^8 square-planar rhodium(I) complex. It further suggests that development of the σ bond (and not the π bond) is of critical importance in the formation of the activated complex.[19]

Acknowledgment. Dr. C. A. Tolman made important suggestions relating to the calculation of equilibrium constants.

(13) The much stronger coordination of 1,2-dihaloethylene as compared with 1,1-dihalides may be a consequence of the symmetrical development of both lobes of the π bond: (a) H. W. Quinn, J. S. McIntyre, and D. J. Peterson, *Can. J. Chem.*, 43, 2897 (1965); (b) J. R. Holden and N. C. Baenziger, *J. Am. Chem. Soc.*, 77, 4987 (1955).

(14) Another reasonable interpretation is that the entropy and enthalpy changes reflect differences in the solvation of either the olefins or their complexes. The possibility of measuring a series of equilibrium constants for eq 1 in ethylene glycol, the solvent generally used with silver complexes, has been explored. $acacRh(C_2H_4)_2$ is so sparingly soluble in this liquid that the concentration must be reduced by a factor of 10. The solubility of ethylene is also lower in glycol than in toluene. Because of dilution and the high viscosity of the solutions, equilibration is inconveniently slow. A few measurements with propene gave a value for K_E of 0.06.

(15) M. A. Bennett, *Chem. Rev.*, 62, 611 (1962); I. Jardine and F. J. McQuillin, *J. Chem. Soc., Sect. C*, 458 (1966).

(16) E. Gil-Av and J. Herling, *J. Phys. Chem.*, 66, 1208 (1962).

(17) W. H. Prichard and W. J. Orville-Thomas, *Theoret. Chim. Acta*, 3, 426 (1965).

(18) R. Cramer, *Inorg. Chem.*, 4, 445 (1965).

(19) In a related reaction, H. G. Schuster-Woldan and F. Basolo (*J. Am. Chem. Soc.*, 88, 1657 (1966)) noted the importance of σ-bond formation. They found phosphines (better σ donors) displaced CO from π-$C_5H_5Rh(CO)_2$ faster than phosphites (better π acceptors).

Rates and Mechanism of Substitution Reactions of Nitrosyltetracarbonylmanganese(0) and Trinitrosylcarbonylmanganese(0)

Henning Wawersik[1] and Fred Basolo

Contribution from the Department of Chemistry, Northwestern University, Evanston, Illinois 60201. Received April 3, 1967

Abstract: Kinetic studies for substitution reactions of the five-coordinated compound $MnNO(CO)_4$ and some of its derivatives are reported. The parent compound reacts by a second-order process, whereas the replacement of CO from $MnNO(CO)_3L$ is largely a first-order reaction. Investigations on the last known member of the pseudo-nickel carbonyl series, $Mn(NO)_3CO$, show it to be very reactive. Its rate of reaction depends on the nature and concentration of the reagent.

The compound $MnNO(CO)_4$[2] is isoelectronic and presumably isostructural with $Fe(CO)_5$ which has a trigonal bipyramidal structure.[3] Several five-coordinated metal complexes are known,[4] but the kinetics and mechanism of substitution reactions of these systems have not been extensively examined. Three such studies have been reported. One deals with the reactions of $RCOCo(CO)_4$ with $P(C_6H_5)_3$,[5] another with

(1) Exchange graduate student from the Technischen Hochschule, München, Germany.

(2) P. M. Treichel, E. Pitcher, R. B. King, and F. G. A. Stone, *J. Am. Chem. Soc.*, 83, 2593 (1961).

(3) J. Donohue and A. Caron, *Acta Cryst.*, 17, 663 (1964).

(4) E. L. Muetterties and R. A. Schunn, *Quart. Rev.* (London), 20, 245 (1966).

the acid-induced carbon monoxide exchange with $Fe(CO)_5$,[6] and the most recent with the reaction of $Fe(CO)_4P(C_6H_5)_3$ with $P(C_6H_5)_3$.[7] In all of these cases the reactions take place by a dissociation (SN1) mechanism. Data are reported in this paper in support of a displacement (SN2) mechanism for substitution reactions of $MnNO(CO)_4$.

Also reported here are the few results obtained on substitution reactions of $Mn(NO)_3CO$.[8] This compound is the last known member of the pseudo-nickel carbonyl series $Ni(CO)_4$, $CoNO(CO)_3$, $Fe(NO)_2(CO)_2$, $Mn(NO)_3CO$, and $Cr(NO)_4$. The results obtained are compared with those made on the corresponding nickel,[9] cobalt,[10] and iron[11] compounds.

Experimental Section

Compounds and Solvents. The solvents used were purified by distillation and carefully dried. The reagents $P(C_6H_6)_3$, $As(C_6H_5)_3$, and $P(OC_6H_5)_3$ were Eastman Organic Chemicals. The first two compounds were purified by recrystallization from absolute methanol, and $P(OC_6H_5)_3$ was distilled over sodium. Aldrich Chemical Co. was the source of $P(n\text{-}C_4H_9)_3$ which was distilled at reduced pressures and under nitrogen before use.

The compounds $MnNO(CO)_4$ and $Mn(NO)_3CO$ were prepared by the methods described earlier.[12] Preparations of derivatives for $MnNO(CO)_4$ not previously reported are described here. The mono[13] and bis[14] $P(C_6H_5)_3$ derivatives were prepared as described in the literature. Compounds of the type $Mn(NO)_3L$ were not isolated but were demonstrated to be present in solution by comparing their infrared spectra with that for $Mn(NO)_3P(C_6H_5)_3$.[8] The infrared spectra in the C–O and N–O stretching regions for $MnNO(CO)_4$ and its derivatives are shown in Table I, and Table II gives this information for $Mn(NO)_3CO$ and its derivatives.

Table I. Infrared Spectra in C–O and N–O Regions for $MnNO(CO)_4$ and Its Derivatives in p-Xylene (cm^{-1})

	ν_{CO}			ν_{NO}
$MnNO(CO)_4$	2106 w,	2034 s,	1979 s	1763 s
$MnNO(CO)_3P(C_6H_5)_3$	2034 s,	1972 m,	1925 s	1712 s
$MnNO(CO)_2[P(C_6H_5)_3]_2$		1952 m,	1868 ss	1662 s
$MnNO(CO)_3P(n\text{-}C_4H_9)_3$	2034 s,	1964 m,	1912 s	1702 s
$MnNO(CO)_2[P(n\text{-}C_4H_9)_3]_2{}^a$		1937 m,	1854 ss	1657 s
$MnNO(CO)_3P(OC_6H_6)_3$	2050 s,	1987 m,	1940 s	1731 s
$MnNO(CO)_2[P(OC_6H_5)_3]_2$		1985 m,	1881 ss	1702 s
$MnNO(CO)_3As(C_6H_5)_3$	2036 s,	1968 m,	1925 s	1712 s

^{a} In Nujol since bands overlap with p-xylene absorptions.

Preparation of Compounds. All operations were carried out using anhydrous solvents and under nitrogen with the careful exclusion of oxygen.

The compounds $MnNO(CO)_3P(OC_6H_5)_3$ and $MnNO(CO)_2[P(OC_6H_5)_3]_2$ were prepared by the reaction of $MnNO(CO)_4$ with $P(OC_6H_5)_3$ in p-xylene solution. A reaction mixture containing 150 mg of $MnNO(CO)_4$ and 0.5 ml of $P(OC_6H_5)_3$ in 50 ml of p-xylene was heated for 2 hr at 120°. After cooling the solution to room temperature, the solvent was removed at reduced pressure. The residue was dissolved in 5 ml of hexane and the solution passed through a filter. Upon standing in an ice bath for 3 days, red

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(7) E. E. Siefert and R. J. Anglelici, *J. Organometal. Chem.* (Amsterdam), **8**, 374 (1967).

(8) C. G. Barraclough and J. Lewi, *J. Chem. Soc.*, 4842 (1960); W. Hieber, W. Beck, and H. Tengler, *Z. Naturforsch.*, **15b**, 411 (1960).

(9) L. R. Kangas, R. F. Heck, P. M. Henry, S. Breitschaft, E. M. Thorsteinson, and F. Basolo, *J. Am. Chem. Soc.*, **88**, 2334 (1966).

(10) E. M. Thorsteinson and F. Basolo, *ibid.*, **88**, 3929 (1966); *Inorg. Chem.*, **5**, 1691 (1966); A. Foffani, private communication.

(11) D. Morris, private communication.

(12) H. Wawersik and F. Basolo, *Inorg. Chem.*, **6**, 1066 (1967).

(13) R. F. Lambert and J. D. Johnson, *Chem. Ind.* (London), 1267 (1960).

(14) W. Hieber and H. Tengler, *Z. Anorg. Allgem. Chem.*, **318**, 136 (1962).

Table II. The N–O Stretching Frequencies (cm^{-1}) of $Mn(NO)_3CO$ and Its Derivatives in p-Xylene

	ν_{NO}	
$Mn(NO)_3CO^a$	1824 m,	1731 ss
$Mn(NO)_3P(C_6H_5)_3$	1780 w,	1690 ss
$Mn(NO)_3P(n\text{-}C_4H_9)_3$	1774 w,	1680 ss
$Mn(NO)_3P(OC_6H_5)_3$	1788 w,	1705 ss
$Mn(NO)_3As(C_6H_5)_3$	1792 w,	1692 ss

^{a} ν_{CO}, 2095 cm^{-1}.

crystals of $MnNO(CO)_2[P(OC_6H_5)_3]_2$ separated from solution, mp 95–97°.

Anal. Calcd for $MnNO(CO)_2[P(OC_6H_5)_3]_2$: C, 59.93; H, 3.97; N, 1.84. Found: C, 58.66; H, 3.71; N, 1.89.

The mother liquor from this low yield of the bis compound was chromatographed on alumina with hexane. Concentration of the eluent did not yield a product so that the solvent was removed at reduced pressure. The resulting oil was kept under high vacuum for 18 hr. With considerable difficulty the oil was caused to crystallize, giving 230 mg (63% yield) of monosubstituted product, mp 42–46°.

Anal. Calcd for $MnNO(CO)_3P(OC_6H_5)_3$: C, 52.63; H, 3.15; N, 2.92. Found: C, 51.88; H, 3.08; N, 3.02.

The synthesis of $MnNO(CO)_2[P(n\text{-}C_4H_9)_3]_2$ was achieved by heating at 120° for ~100 hr 50 ml of a p-xylene solution containing 170 mg of $MnNO(CO)_4$ and 1.3 ml of $P(n\text{-}C_4H_9)_3$. After concentration to dryness at reduced pressure, the residue was dissolved in 30 ml of methanol and filtered. The filtrate was kept at −78° for 24 hr during which time yellow crystals of the product separated from solution. These were recrystallized from methanol, collected on a filter, and dried at room temperature under vacuum. A yield of 360 mg (83%) of the bis compound, mp 50–51°, was obtained which is very soluble in organic solvents.

Anal. Calcd for $MnNO(CO)_2[P(n\text{-}C_4H_9)_3]_2$: C, 57.24; H, 9.28; N, 2.57; mol wt, 545.6. Found: C, 56.43; H, 9.72; N, 2.53; mol wt, 528.

Kinetic Studies. Purified anhydrous p-xylene was used as the solvent in all of the experiments. The reaction mixtures were kept at constant (±0.1°) temperature, in the dark, and under an atmosphere of nitrogen during the kinetic runs. All of the kinetics were carried out under pseudo-first-order conditions, using at least a tenfold excess of reagent. The rates of reaction were followed spectrophotometrically as described below. Measurements were usually made over a period of three half-lives. All reactions went to completion. The data gave good linear plots of log $(A - A_\infty)$ vs. t, where t is time, A is the absorption at time t, and A_∞ is the absorption at infinite time. Estimated rate constants were reproducible to within 10% or better.

The rates of reaction of $MnNO(CO)_4$ and its derivatives were followed by monitoring changes in the infrared spectra of the reaction mixtures. This was done by observing changes in the C–O and N–O stretching regions of the spectra to record the disappearance of starting material and/or appearance of product. The reaction flasks were kept under a slight positive N_2 pressure in order to avoid the introduction of O_2 when samples were removed for infrared measurements by means of a syringe.

This procedure could not be used for the much faster reactions of $Mn(NO)_3CO$. The rates of reaction were decreased by using lower concentrations of reactants, and this required that the rates be followed by recording changes in optical densities at 480 mμ. This was done using a Cary 14 equipped with a thermostated cell compartment and a quartz cell of 10-cm length. This was flushed with N_2, and then 25 ml of a freshly prepared solution of $Mn(NO)_3CO$ in p-xylene was introduced using a gas-tight syringe. After a few minutes the solution was at constant temperature and 1 ml of a p-xylene solution of the reagent was added by means of a syringe. The solutions were rapidly mixed by shaking the cell and the change in absorbance was recorded.

Results

The infrared spectra in the C–O and N–O stretching regions for $MnNO(CO)_4$ and its derivatives are given in Table I, and the same is shown for $Mn(NO)_3CO$ in Table II.

The experimental rate constants, k_{obsd}, and the estimated second-order rate constants, k_2, are collected in

Table III. Rate Constants for Reaction 1 in p-Xylene at 50° ([MnNO(CO)4] = 0.0012 M)

L	[L], M	k_{obsd}, sec^{-1}	k_2, M^{-1} sec^{-1}
P(C$_6$H$_5$)$_3$[a]	6.55 × 10^{-3}	1.6 × 10^{-6}	2.5 × 10^{-3}
P(C$_6$H$_5$)$_3$	3.25 × 10^{-2}	7.1 × 10^{-6}	2.2 × 10^{-3}
P(C$_6$H$_5$)$_3$	1.34 × 10^{-1}	3.1 × 10^{-4}	2.3 × 10^{-3}
P(C$_6$H$_5$)$_3$[b]	...	...	4.4 × 10^{-3}
P(C$_6$H$_5$)$_3$[c]	...	...	1.1 × 10^{-2}
P(OC$_6$H$_5$)$_3$	5.02 × 10^{-2}	8.7 × 10^{-6}	1.7 × 10^{-4}
P(OC$_6$H$_5$)$_3$	8.05 × 10^{-2}	1.4 × 10^{-6}	1.7 × 10^{-4}
P(n-C$_4$H$_9$)$_3$	1.06 × 10^{-2}	9.4 × 10^{-4}	8.9 × 10^{-2}
As(C$_6$H$_5$)$_3$	8.3 × 10^{-2}	3.0 × 10^{-6}	3.6 × 10^{-6}
As(C$_6$H$_5$)$_3$	1.5 × 10^{-1}	4.5 × 10^{-6}	3.0 × 10^{-6}

[a] [MnNO(CO)4] = 0.0004 M. [b] 60°. [c] 70°; values of k_2 for b and c estimated from three runs each. $\Delta H^{\ddagger} = 19 \pm 1$ kcal/mole; $\Delta S^{\ddagger} = -11 \pm 3$ eu.

Table IV. Rate Constants for Reaction 2 in p-Xylene at 120° ([MnNO(CO)3L] = 0.0012 M)

L	[L], M	k_{obsd}, sec^{-1}	k_1, sec^{-1} [a]	k_2, M^{-1} sec^{-1} [a]
P(C$_6$H$_5$)$_3$	8.07 × 10^{-3}	12.7 × 10^{-6}	1.3 × 10^{-6}	1.2 × 10^{-6}
P(C$_6$H$_5$)$_3$	3.89 × 10^{-2}	13.1 × 10^{-6}	...	...
P(C$_6$H$_5$)$_3$	1.52 × 10^{-1}	14.4 × 10^{-6}	...	...
P(n-C$_4$H$_9$)$_3$	1.31 × 10^{-2}	5.3 × 10^{-6}	4.7 × 10^{-6}	4.1 × 10^{-5}
P(n-C$_4$H$_9$)$_3$	6.35 × 10^{-2}	7.3 × 10^{-6}	...	...
P(n-C$_4$H$_9$)$_3$	1.94 × 10^{-1}	12.7 × 10^{-6}	...	...
P(OC$_6$H$_5$)$_3$	8.25 × 10^{-3}	4.9 × 10^{-6}	4.0 × 10^{-6}	...
P(OC$_6$H$_5$)$_3$	6.32 × 10^{-2}	3.5 × 10^{-6}	...	...
P(OC$_6$H$_5$)$_3$	1.54 × 10^{-1}	4.2 × 10^{-6}	...	...

[a] See eq 3 for meaning of k_1 and k_2. Values of k_1 are the nonzero intercepts of the plots of k_{obsd} vs. [L], and values of k_2 are obtained from the slope of the lines.

Table V. Rate Constants for Reaction 4 in p-Xylene ([MnNO(CO)3P(OC6H5)3] = 0.001 M)

Temp, °C	L	[L], M	k_{obsd}, sec^{-1}	k_2, M^{-1} sec^{-1}
50	P(n-C$_4$H$_9$)$_3$	2.17 × 10^{-2}	1.0 × 10^{-6}	4.6 × 10^{-6}
50	P(n-C$_4$H$_9$)$_3$	1.57 × 10^{-1}	6.8 × 10^{-6}	4.3 × 10^{-6}
50	P(n-C$_4$H$_9$)$_3$	4.18 × 10^{-1}	1.8 × 10^{-6}	4.3 × 10^{-6}
80	P(n-C$_4$H$_9$)$_3$[a]	2.27 × 10^{-2}	8.3 × 10^{-6}	3.6 × 10^{-4}
80	P(n-C$_4$H$_9$)$_3$	1.71 × 10^{-1}	6.2 × 10^{-6}	3.6 × 10^{-4}
80	P(n-C$_4$H$_9$)$_3$	4.13 × 10^{-1}	1.5 × 10^{-4}	3.6 × 10^{-4}
80	P(C$_6$H$_5$)$_3$	4.46 × 10^{-2}	Too slow	...
80	P(C$_6$H$_5$)$_3$	1.32 × 10^{-1}	5.2 × 10^{-7}	3.9 × 10^{-6}
80	P(C$_6$H$_5$)$_3$	4.3 × 10^{-1}	1.8 × 10^{-6}	4.2 × 10^{-6}

[a] $\Delta H^{\ddagger} = 15 \pm 2$ kcal/mole; $\Delta S^{\ddagger} = -30 \pm 5$ eu.

Table VI. Rate Constants for Reaction 5 in p-Xylene at 22° ([Mn(NO)3CO] = 5 × 10^{-6} M)

L	[L], M	k_{obsd}, sec^{-1}	k_2, M^{-1} sec^{-1}
As(C$_6$H$_5$)$_3$	6.4 × 10^{-4}	7.3 × 10^{-3}	5.6[a]
As(C$_6$H$_5$)$_3$	1.9 × 10^{-3}	1.4 × 10^{-2}	...
As(C$_6$H$_5$)$_3$	3.8 × 10^{-3}	2.5 × 10^{-2}	...
P(C$_6$H$_5$)$_3$	5.9 × 10^{-4}	3.2 × 10^{-2}	54[b]
P(n-C$_4$H$_9$)$_3$	5.5 × 10^{-4}	>10^{-1}	>200[b]

[a] Estimated from slope of line of plot of k_{obsd} vs. [As(C$_6$H$_6$)$_3$]. [b] Estimated assuming first-order dependence on reagent.

Table III for the reaction of MnNO(CO)4 with various reagents. Also included are rates at different temperatures and activation parameters for its reaction with P(C$_6$H$_5$)$_3$.

Rate constants for the formation of the bis compounds MnNO(CO)2L2 are given in Table IV, and Table V contains data on the ligand exchange reactions of MnNO(CO)3L.

Table VI contains the rate constants for the reactions of Mn(NO)3CO with different reagents.

Discussion

Extensive investigations have been made of the kinetics and mechanism of substitution reactions of metal complexes having either octahedral or square-planar structures. These studies show that the coordination number and the geometry of the metal complex play a major role in its mechanism of reaction. Thus octahedral substitution appears to involve primarily a dissociative process, whereas square-planar substitution takes place by an associative process.[15] In both cases a five-coordinated active intermediate or activated complex is involved. This then adds a ligand in octahedral substitutions and loses a ligand in square-planar substitutions in order to form products.

Stable five-coordinated metal complexes are known[4] and afford one an opportunity to investigate substitution reactions in some of these systems. Quantitative studies on such metal compounds containing unidentate ligands are not extensive, but the results obtained support trigonal bipyramidal substitution by a dissociation mechanism.[5-7] However, the data in Table III clearly show that the rate of reaction 1 is second order, being

$$MnNO(CO)_4 + L \longrightarrow MnNO(CO)_3L + CO \qquad (1)$$

first order in the concentrations of both the substrate and the reagent. This suggests that reaction takes place by an S_N2 displacement process. Additional support is afforded this mechanism by the observation that the reaction between Mn(NO)(CO)4 and P(C$_6$H$_5$)$_3$ has a negative entropy of activation. Such a result implies there is a net increase in bonding in the formation of the transition state, and negative entropies of activation are often observed for displacement reactions.[16] For poor nucleophiles a dissociative reaction path may contribute to the total rate, and this appears to be true for the reagent As(C$_6$H$_5$)$_3$ as it was for its reaction with CoNO(CO)$_3$.[10]

The reagent reactivity toward MnNO(CO)4 is seen to decrease in the order P(n-C$_4$H$_9$)$_3$ (40) > P(C$_6$H$_5$)$_3$ (1) > P(OC$_6$H$_5$)$_3$ (0.08) > As(C$_6$H$_5$)$_3$ (0.015). The numbers in parentheses are the relative rates of reaction at 50° assigning a rate of one to P(C$_6$H$_5$)$_3$. This order qualitatively parallels that reported earlier[10] for the nucleophilic strengths at 25° toward CoNO(CO)$_3$: P(n-C$_4$H$_9$)$_3$ (90) > P(C$_6$H$_5$)$_3$ (1) > P(OC$_6$H$_5$)$_3$ (0.03) > As(C$_6$H$_5$)$_3$ (0.002). Therefore, it appears that manganese, like cobalt, in the nitrosyl carbonyl is a class

(15) C. H. Langford and H. B. Gray, "Ligand Substitution Processes," W. A. Benjamin, Inc., New York, N. Y., 1965.
(16) U. Belluco, R. Ettore, F. Basolo, R. G. Pearson, and A. Turco, *Inorg. Chem.*, 5, 591 (1966).

(b)[17] metal or soft acid[18] and reacts preferentially with soft bases.

That the isoelectronic and isostructural compounds Fe(CO)$_5$ and MnNO(CO)$_4$ react by different mechanisms is similar to the behavior of the corresponding compounds Ni(CO)$_4$[9] and CoNO(CO)$_3$.[10] The metal carbonyls tend to react by a first-order process, whereas the corresponding metal nitrosyl carbonyls tend to react by a second-order process. This was explained[11] on the basis of the localization of a pair of electrons on the nitrosyl group in the transition state, thus permitting the addition of a pair of electrons by the nucleophile to the system. Such a process would be more difficult for a carbonyl group because carbon is less electronegative than nitrogen and because nitrogen is believed to have a formal positive charge in the metal nitrosyl carbonyls.

It is of interest to briefly comment on the stereochemistry of the displacement reactions of MnNO(CO)$_4$. An examination of molecular models shows that the reaction paths represented in Figure 1 are possible. From this it is apparent that the assumed six-coordinated species II may readily yield products with different structures. In addition this may be further complicated by the fact that five-coordinated systems often have nonrigid structures.[4] For example, ^{13}C nmr shows that all of the carbonyls in Fe(CO)$_5$ are equivalent.[19] If this also is true for MnNO(CO)$_4$ and its derivatives, then it is clear that rearrangements will occur readily to produce the more stable isomers. Structure IV has been assigned[14] MnNO(CO)$_3$P(C$_6$H$_5$)$_3$ on the basis of its dipole moment compared to that for Fe(CO)$_4$P(C$_6$H$_5$)$_3$.

Data in Table IV show that the rates of reaction 2 are much slower than are the rates of reaction 1. This is the usual behavior of metal carbonyls;[20] that is, the

$$\text{MnNO(CO)}_3\text{L} + \text{L} \longrightarrow \text{MnNO(CO)}_2\text{L}_2 + \text{CO} \qquad (2)$$

replacement of the first CO with phosphines or phosphites takes place more readily than do additional replacements. It appears that the remaining CO's become more firmly held because of increased metal-to-carbon π bonding.

In addition to this normal behavior, the data in Table IV show an unexpected result. Except for the best nucleophile, P(n-C$_4$H$_9$)$_3$, the rates of reaction are almost independent of reagent concentration.

For P(n-C$_4$H$_9$)$_3$ the experimentally observed rate constant increases with increasing reagent concentration and appears to follow the two-term rate law given by eq 3. The reagent-independent path, k_1, is believed to

$$k_{\text{obsd}} = k_1 + k_2[\text{L}] \qquad (3)$$

take place by a dissociation mechanism, whereas the k_2 path is the direct reagent displacement path. Except for steric factors, the contribution of the k_2 path to the observed rate of reaction will be greater for the better nucleophiles. We see this to be true in that of the reagents used the largest contribution to the total rate is made by the best nucleophile, P(n-C$_4$H$_9$)$_3$, and the

(17) S. Ahrland, J. Chatt, and N. R. Davies, *Quart. Rev.* (London), 12, 265 (1958).
(18) R. G. Pearson, *J. Am. Chem. Soc.*, 85, 3533 (1963).
(19) R. Bramley, B. N. Figgis, and R. S. Nyholm, *Trans. Faraday Soc.*, 58, 1893 (1962).
(20) F. Basolo and R. G. Pearson, "Mechanisms of Inorganic Reactions," John Wiley and Sons, New York, N. Y., 1967, Chapter 7.
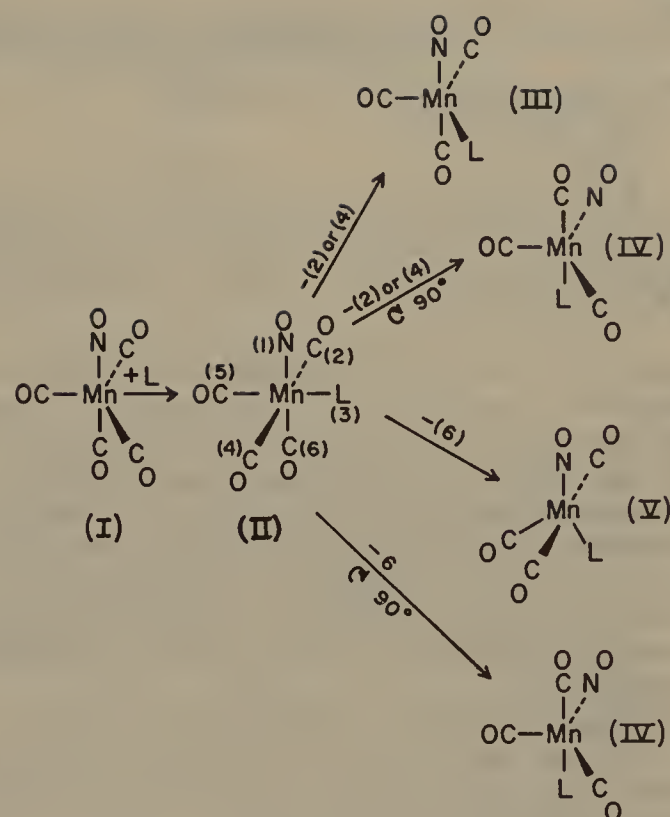
Figure 1. Possible stereochemistry of the reaction of MnNO(CO)$_4$ to yield MnNO(CO)$_3$L. This assumes that CO(5) in II is not replaced because it is *trans* to L and presumably is less reactive than the other CO's: F. Basolo and A. Wojcicki, *J. Am. Chem. Soc.*, 83, 520 (1961); see also J. Lewis, J. R. Miller, B. H. Robinson, P. W. Robinson, and A. Wojcicki, *Chem. Commun.*, 379 (1967); H. D. Kaez, R. Bow, D. Hendrickson, and J. M. Smith, Abstracts, 153rd National Meeting of the American Chemical Society, Miami Beach, Fla., April 1967.

poorest, P(OC$_6$H$_5$)$_3$, has no effect up to a concentration of 0.15 M.

What was unexpected is that a major portion of the reaction of MnNO(CO)$_3$L takes place by a dissociation process. All previous observations[10] were that, except for very poor nucleophiles, metal nitrosyl carbonyls react primarily by a displacement process. However, these observations were made only on four-coordinated systems. It seems reasonable that steric retardation of bimolecular displacement reactions would increase with increasing coordination number of the metal. This is perhaps what is responsible for the smaller contribution of the k_2 path of the rate of reaction of the five-coordinated compound MnNO(CO)$_3$L to give MnNO(CO)$_2$L$_2$. Alternatively, it may be that for some electronic reason the presence of ligand L in the compound stabilizes a four-coordinated transition state of the type MnNO(CO)$_2$L and permits reaction by a dissociation process.

The rates of dissociation of MnNO(CO)$_3$L with changes in L decrease in the order P(C$_6$H$_5$)$_3$ > P(n-C$_4$H$_9$)$_3$ > P(OC$_6$H$_5$)$_3$, which corresponds to that found for the reactions of Ni(CO)$_3$L[21] and of Mn(CO)$_4$LBr.[22] Another comparison is that MnNO(CO)$_3$P(C$_6$H$_5$)$_3$ reacts with P(C$_6$H$_5$)$_3$ at 120° at a rate approximately 100 times faster than that estimated for the same reaction of its isoelectronic and isostructural compound Fe(CO)$_4$P(C$_6$H$_5$)$_3$.[7] This is somewhat surprising because the Mn–C bond strength is expected to be greater than

(21) L. S. Meriwether and M. L. Fiene, *J. Am. Chem. Soc.*, 81, 4200 (1959).
(22) R. J. Angelici and F. Basolo, *Inorg. Chem.*, 2, 728 (1963).

Table VII. Stretching Force Constants for C–O and N–O in Pseudo-Nickel Carbonyl Series and Rates of Reaction

	$Ni(CO)_4$	$CoNO(CO)_3$	$Fe(NO)_2(CO)_2$		$Mn(NO)_3CO$
F_{CO}, 10^5 dynes/cm [a]	17.23	17.04	17.06		17.43
F_{NO}, 10^5 dynes/cm [a]	...	14.44	14.12		13.75
k_1, sec^{-1}	1.5×10^{-2} [b]	$\sim 10^{-7}$ [c]	$\sim 10^{-7}$ [c]		$\sim 4 \times 10^{-3}$ [c]
k_2, M^{-1} sec^{-1} [d]	...	1×10^{-3}	1×10^{-3}		54

[a] From G. R. Van Hecke and W. D. Horrocks, Jr., *Inorg. Chem.*, **5**, 1960 (1966). [b] Reaction with $P(C_6H_5)_3$ from ref 9. [c] Extrapolated nonzero intercept for reaction with $As(C_6H_5)_3$ from ref 10, 11, and Table VI. [d] Second-order rate constants for reactions with $P(C_6H_5)_3$ from ref 10, 11, and Table VI.

that of Fe–C because of the smaller nuclear charge on manganese permitting more metal-to-carbon π bonding. Relative to CO, the greater activating influence of NO may, therefore, be related largely to its influence on stabilizing the transition state for reaction. The product $MnNO(CO)_2[P(C_6H_5)_3]_2$ has a trigonal bipyramidal structure with the phosphines in axial positions.[14,23] Unfortunately, as stated above, the structures of these reaction products cannot be used to assign mechanisms of reaction.

The rates of reaction 4, where L is $P(n\text{-}C_4H_9)_3$ or $P(C_6H_5)_3$, are given in Table V. The rates of reaction depend on L, and again it is seen that $P(n\text{-}C_4H_9)_3$ is a

$$MnNO(CO)_3P(OC_6H_5)_3 + L \longrightarrow$$
$$MnNO(CO)_3L + P(OC_6H_5)_3 \quad (4)$$
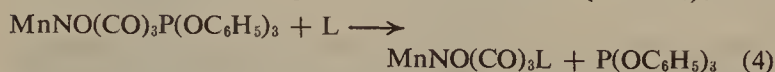
better reagent than is $P(C_6H_5)_3$. The observed second-order kinetics suggests that the reactions take place by an S_N2 process. That reaction takes place with a negative entropy of activation also lends support to such a mechanism.[16]

Thus, it is of interest to note that reaction 2 takes place largely by a dissociation mechanism and reaction 4 by a displacement process. It was suggested that steric retardation in reaction 2 may be involved to such an extent that the reaction proceeds by dissociation. The results show that such an argument cannot apply to reaction 4. Perhaps here the steric retardation is less, because the leaving group is the bulky phosphite. Assuming it is only weakly bonded to manganese in the transition state, this provides room for attack by the entering nucleophile. Less room would be available when the smaller CO is the leaving group, as per reaction 2. Another factor may be that CO is more firmly bonded to Mn in $MnNO(CO)_3L$ than is L. This means that more drastic conditions are needed to replace CO, and at these higher temperatures the dissociation process predominates.

Finally, a few kinetic studies (Table VI) were made of reaction 5, where L is $As(C_6H_5)_3$, $P(C_6H_5)_3$, or $P(n\text{-}C_4H_9)_3$. The experiments were difficult to perform be-

$$Mn(NO)_3CO + L \longrightarrow Mn(NO)_3L + CO \quad (5)$$

cause of the extreme sensitivity of $Mn(NO)_3CO$ and its rapid rate of reaction, However, the results leave no doubt that the rate of reaction depends on the nature and concentration of the reagent. On the basis of the limited data available, it appears that the reaction of $Mn(NO)_3CO$ with $As(C_6H_5)_3$ follows a two-term rate law of the type shown by eq 3. The same result was found for its reaction with $CoNO(CO)_3$.[10] It is assumed that the phosphines, which are better nucleophiles, react primarily by the k_2 path.

(23) J. H. Enemark and J. A. Ibers, private communication.

Kinetic investigations have now been made for reactions of all the known compounds of the pseudo-nickel carbonyl series. Some of the data obtained are collected in Table VII along with the estimated C–O and N–O stretching force constants. The stereochemistries of these compounds are the same, but the formal charges on the metals decrease in the order Ni(0), Co(−I), Fe(−II), Mn(−III). On this basis one might expect a continuous increase in metal-to-carbon π bonding across the series to parallel the increase in formal negative charge. However, the C–O force constants suggest that this happens only on the addition of the first NO in going from $Ni(CO)_4$ to $CoNO(CO)_3$. Further addition of NO is accompanied by an increase in the C–O force constant, implying a decrease in metal-to-carbon π bonding. It appears that the reason for this is that NO is a better π bonder than CO. Thus the extent of metal-to-carbon π bonding decreases with added NO, in spite of the increase in negative formal charge. This is supported by the continuous decrease observed in the NO force constants with added NO in the series.

These results suggest that the metal-to-carbon π bonding and presumably M–C bond strength in the series of compounds vary in the order Ni < Co $\sim$ Fe > Mn. It is to be expected that for first-order processes, k_1 in Table VII, where the M–C bond is of major importance, the rates of reaction should parallel their bond strengths. A quantitative comparison is not possible because the estimated data are not sufficiently reliable. However, a good qualitative correspondence is found with the reactions of the Ni and Mn compounds being fast and those of Co and Fe slow.

No second-order path has been observed for reactions of $Ni(CO)_4$ with a variety of reagents.[9] Although a similar low-energy first-order path is available for reactions of $Mn(NO)_3CO$, it also reacts readily by a second-order path. As mentioned above the presence of NO in place of CO in these systems markedly enhances the tendency for reaction by means of a displacement process. This and the weaker M–C bond strength can account for the much larger value of k_2 for $Mn(NO)_3CO$ relative to $CoNO(CO)_3$. What is not clear is that the second-order rates of reaction of the cobalt and the iron compounds are about the same. It might be expected that because the iron compound contains two NO's this would induce a more facile displacement process relative to the cobalt system with only one NO.

Organic and Biological Chemistry

Activation Parameters for Semicarbazone Formation[1]

Rama Kant Chaturvedi and E. H. Cordes[2]

Contribution No. 1488 from the Department of Chemistry, Indiana University, Bloomington, Indiana 47401. Received March 6, 1967

Abstract: Activation parameters for the attack of semicarbazide on *p*-hydroxybenzaldehyde catalyzed by the hydrated proton, by formic acid, and by the solvent have been evaluated from third-order rate constants measured at each of three temperatures in aqueous solution, ionic strength 0.50. For each catalyst, values of $\Delta H^{\pm}$ near 9 kcal/mole have been obtained. Values of $\Delta S^{\pm}$ become progressively more negative as the acidity of the catalyst is decreased. Thus, the relative efficiency of these catalysts for the attack of semicarbazide on *p*-hydroxybenzaldehyde is principally a reflection of changes in the entropy of activation. The equilibrium constant for carbinolamine formation from semicarbazide and *p*-chlorobenzaldehyde has been evaluated as a function of temperature and values of ΔH° of −2.3 kcal/mole and ΔS° of −5.4 eu obtained. Activation parameters for *p*-chlorobenzaldehyde semicarbazone formation under conditions of rate-determining carbinolamine dehydration and in dilute solutions of semicarbazide in which little of the substrate is converted to the carbinolamine in the preequilibrium reaction were determined: $\Delta H^{\pm} = 3.9$ kcal/mole and $\Delta S^{\pm} = -22$ eu. From these values and those for *p*-chlorobenzaldehyde carbinolamine formation, activation parameters for the dehydration of this carbinolamine were evaluated: $\Delta H^{\pm} = 6.2$ kcal/mole and $\Delta S^{\pm} = -16.6$ eu. These latter values are in accord with those obtained directly from the temperature dependence of the rate of *p*-nitrobenzaldehyde semicarbazone formation under conditions of rate-determining carbinolamine decomposition and in solutions of semicarbazide sufficiently concentrated to convert substantially all of the aldehyde to the carbinolamine in a preequilibrium reaction.

Mechanism and catalysis for nucleophilic reactions at the carbonyl carbon atom and for the reverse reaction have been extensively explored in the last few years.[3] A comprehensive summary has been prepared by Jencks.[4] In contrast, little work has been directed toward the evaluation of activation parameters for these reactions in this same time period. There have been a number of studies concerned with activation parameters for semicarbazone and oxime formation carried out some years ago.[5-10] For the most part, these studies require clarification and reinterpretation since (a) they were carried out before it was clearly established that different steps in the reaction sequence were rate determining at different values of pH[3a] and (b) activation parameters were evaluated from second-order rate constants which are pH dependent; therefore, the entropies of activation are themselves pH de-

pendent and not very revealing. A recent evaluation of activation parameters for nitrone formation does not suffer from either of these disadvantages although serious questions about the assignation of rate-determining step can be raised[11] (see below). In an effort to provide a basis for understanding earlier results more clearly and to provide information of a type not yet available in the literature, we have evaluated a rather complete set of activation parameters for semicarbazone formation from benzaldehydes. Activation parameters for the reverse reactions have recently been reported.[12]

Experimental Section

Materials. Carbonyl compounds were obtained commercially and were either redistilled or recrystallized prior to use. Semicarbazide hydrochloride was recrystallized repeatedly from aqueous ethanol; solutions were prepared and neutralized as required just prior to use in kinetic runs or equilibrium constant measurements. Potassium chloride and formic acid were reagent grade and were employed without further purification. Distilled water was used throughout.

Kinetic measurements were carried out spectrophotometrically with the aid of a Zeiss PMQ II spectrophotometer equipped with a cell holder through which water from a thermostated water bath was continuously circulated. Temperature was regulated with the aid of a Bronwill thermostated heater and circulator. Temperatures were measured using a calibrated Beckman thermometer. On repeated occasions, temperatures were measured in the reaction vessels within the cell housing of the spectrophotometer; these were ordinarily within 0.05° of the value for the water bath. All reactions were carried out at an ionic strength of 0.50 maintained with KCl. Reactions were run in aqueous solution containing 3.3% ethanol. Activation parameters were obtained from Arrhenius plots and the appropriate ancillary equations. Slopes of all Arrhenius plots were obtained by unweighted least-squares analysis.

(1) Supported by Grant AM 08232 from the National Institutes of Health.

(2) Career Development Awardee of the National Institutes of Health.

(3) Leading references include: (a) W. P. Jencks, *J. Am. Chem. Soc.*, **81**, 475 (1959); (b) B. M. Anderson and W. P. Jencks, *ibid.*, **82**, 1773 (1960); (c) E. H. Cordes and W. P. Jencks, *ibid.*, **84**, 826, 832 (1962); (d) E. H. Cordes and W. P. Jencks, *ibid.*, **84**, 4319 (1962); (e) R. L. Reeves, *ibid.*, **84**, 3332 (1962); (f) E. H. Cordes and W. P. Jencks, *ibid.*, **85**, 2843 (1963); (g) K. Koehler, W. A. Sandstrom, and E. H. Cordes, *ibid.*, **86**, 2413 (1964); (h) L. do Amaral, W. A. Sandstrom, and E. H. Cordes, *ibid.*, **88**, 2225 (1966); (i) J. E. Reimann and W. P. Jencks, *ibid.*, **88**, 3973 (1966); (j) R. L. Reeves and W. F. Smith, *ibid.*, **85**, 724 (1963); (k) R. L. Reeves, *J. Org. Chem.*, **30**, 3129 (1965); (l) R. B. Martin, *J. Phys. Chem.*, **68**, 1369 (1964).

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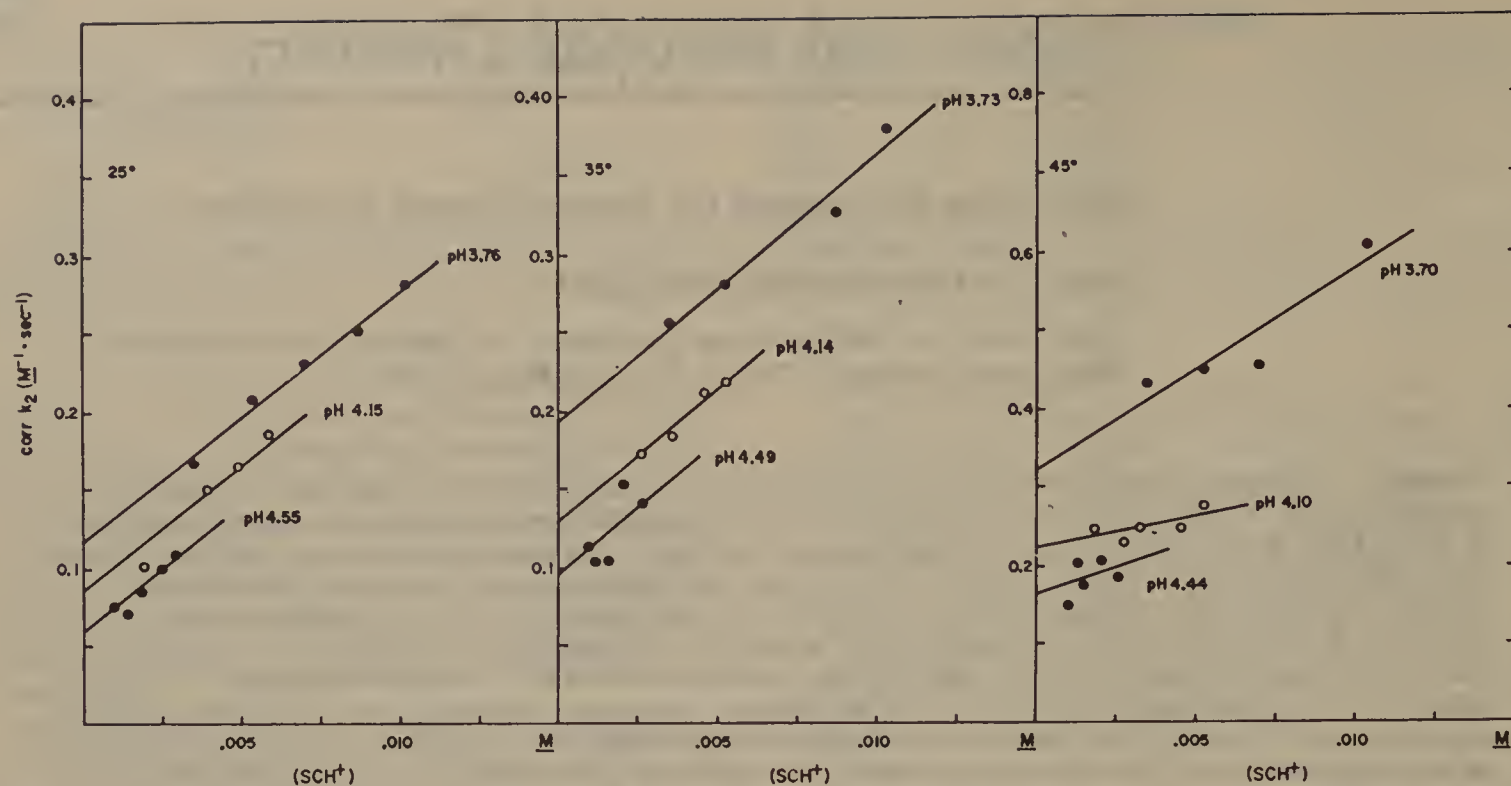
Figure 1. Second-order rate constants for *p*-hydroxybenzaldehyde semicarbazone formation corrected to constant values of pH (see text) plotted against the concentration of the conjugate acid of semicarbazide. At 25 and 35°, the slopes at each value of pH are those calculated by least-squares treatment for the data under the most acidic conditions. At 45°, the slopes were calculated for each set of data independently.

All kinetic runs were carried out in the presence of semicarbazide present in sufficient excess so that first-order kinetics were obtained throughout the course of each run. First-order rate constants were obtained as usual by determination of half-times from semilogarithmic plots of $(OD_\infty - OD_t)$ against time and the expression $k_{obsd} = 0.693/t_{1/2}$. Evaluation of higher order rate constants is not completely trivial, and we discuss each case in turn. For the reaction of *p*-hydroxybenzaldehyde with semicarbazide under mildly acidic conditions, in which attack of the amine on the carbonyl compound is the rate-determining step, second-order rate constants were obtained by dividing first-order constants by the concentration of semicarbazide in the free base form. Calculation of third-order rate constants was accomplished essentially as previously described.[3d] These reactions have a rate law of the following form: $k_{obsd} = k_0(RNH_2) + k_{H^+}(RNH_2)(H^+) + k_{SCH^+}(RNH_2)(RNH_3^+)$ or $k_2 = k_0 + k_H(H^+) + k_{SCH^+}(RNH_3^+)$ in which k_0, k_{H^+}, and k_{SCH^+} are the third-order rate constants for catalysis by solvent, the hydrated proton, and the conjugate acid of semicarbazide, respectively.[3d] Hence, the data are treated by first plotting the calculated second-order rate constants against the concentration of the protonated semicarbazide. The slopes of such plots are measures of k_{SCH^+} and the intercepts are equal to $k_0 + k_{H^+}(H^+)$. Such plots are indicated in Figure 1. For the data at 25 and 35° in which substantial catalysis was observed at all values of pH, the least-squares slopes were evaluated from the data at the most acidic values of pH employed. These should be the most accurate determinations of k_{SCH^+} since the greatest range of catalyst concentration is obtained under these conditions. Then, applying these least-squares slopes to the data at higher values of pH, least-squares intercepts were evaluated. At 45°, rather little catalysis was observed, and the intercepts were obtained at each value of pH from independent least-squares calculations. No attempt was made to evaluate k_{SCH^+} at this temperature. Third-order rate constants for the solvent and hydrated proton-catalyzed reactions were evaluated from the intercept and slope, respectively, of a plot of these intercepts against the activity of hydrogen ion as determined with the glass electrode. These rate constants were then slightly refined as follows. Usually five kinetic runs were made for each value of pH at each temperature. The actual values of pH for these solutions varied by as much as ±0.03 pH unit from the mean value. Since the procedure just described yields third-order rate constants for the reactions catalyzed by the hydrated proton, it is possible to return to the original data and correct all the second-order rate constants to a constant pH by adding or subtracting, as appropriate, the quantity $k_{H^+}(\Delta H^+)$ in which (ΔH^+) is the difference between the average (H^+) for the group of runs under con-

sideration and the value of (H^+) for each particular run. These corrections are quite small, usually less than 5%. Then, employing the corrected values of the second-order rate constants, refined third-order constants were obtained by repeating the analysis just described.

The reaction of *p*-chlorobenzaldehyde with semicarbazide in neutral or mildly alkaline solutions, conditions in which decomposition of the carbinolamine intermediate is the rate-determining step, has a rate law which is third order over-all: first-order in aldehyde, amine, and the hydrated proton.[3a,b] The third-order rate constant is given by $[k_{obsd}/(RNH_2)(H^+)][1 + K(RNH_2)]$, the term $[1 + K(RNH_2)]$ correcting for the fact that appreciable fractions of the carbonyl compound may be converted to the carbinolamine in a preequilibrium reaction. In this expression, K is the equilibrium constant for carbinolamine formation. Since this quantity was measured at each temperature employed, third-order rate constants could be calculated directly employing the above expression.

The second-order rate constant for decomposition of the carbinolamine derived from *p*-nitrobenzaldehyde and semicarbazide was evaluated from the observed first-order rate constant for *p*-nitrobenzaldehyde semicarbazone formation under neutral or slightly alkaline conditions and in the presence of sufficient semicarbazide to convert substantially all of the carbonyl compound to the carbinolamine in a preequilibrium reaction, from the measured hydrogen ion activity, and from the expression $k_2 = k_{obsd}/(H^+)\alpha$, in which α is the fraction of aldehyde present as carbinolamine.[3b] Values of α were obtained from the known semicarbazide concentrations and the equilibrium constant for *p*-nitrobenzaldehyde carbinolamine formation in 25% ethanol measured by Anderson and Jencks.[3b] Use of this equilibrium constant cannot introduce significant errors into the data since, in all cases, values of α were greater than 0.9.

Equilibrium Constant Measurements. The equilibrium constant for formation of carbinolamine from *p*-chlorobenzaldehyde and semicarbazide was evaluated from the slopes of plots of $[OD_0 - OD]/(RNH_2)$ against OD in which OD_0 is the optical density at 259 mμ of the aldehyde alone and OD is the value observed at this wavelength in the presence of various concentrations of semicarbazide. This somewhat indirect approach was employed since it avoids the necessity of a direct determination of the end point at infinite semicarbazide concentration. Justification for this procedure is straightforward: if OD_0 is the optical density of the aldehyde alone and if OD_∞ is that at infinite concentration of semicarbazide in which all the aldehyde exists as carbinolamine, then it is clear that the actual optical density is given by
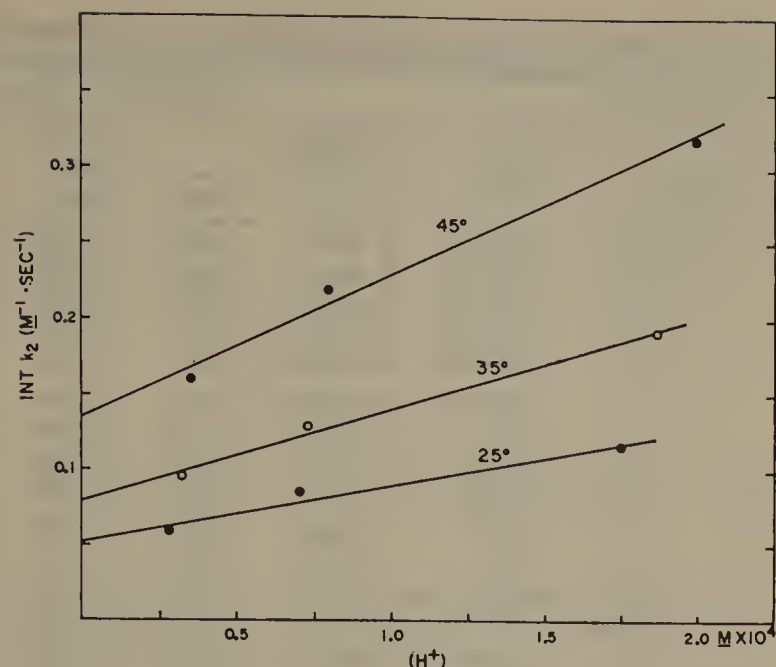
Figure 2. Second-order rate constants for *p*-hydroxybenzaldehyde semicarbazone formation corrected for catalysis by the conjugate acid of semicarbazide (*i.e.*, the intercepts from the plots in Figure 1) plotted against the activity of hydrogen ion for each of three temperatures.

$$OD = f_{ald}(OD_0) + f_{ca}(OD_\infty) \qquad (1)$$

in which f_{ald} is the fraction of total substrate which exists as aldehyde and f_{ca} is that fraction which exists as carbinolamine. Introducing the equilibrium constant for carbinolamine formation, K, eq 1 takes the form

$$OD = \{1/[1 + K(RNH_2)]\}(OD_0) +$$
$$\{K(RNH_2)/[1 + K(RNH_2)]\}(OD_\infty) \qquad (2)$$

Rearranging, we obtain

$$(OD_0 - OD)/(RNH_2) = K(OD) - K(OD_\infty) \qquad (3)$$

Equation 3 forms the basis for the graphical determination of K described above. Values of optical density were determined immediately following the addition of semicarbazide to the aldehyde. Under the conditions of these experiments, extrapolation of the optical densities to zero time to correct for decomposition of the carbinolamine proved unnecessary.

The value of pK_a for the conjugate acid of semicarbazide at 25° and ionic strength 0.50 to 3.65 was confirmed.[3d] The value at this ionic strength and at 35° was determined to be 3.60 as previously described.[3d] The value at 45° was evaluated as 3.55 from the temperature dependence established by the measurements noted above.

Values of pH were determined with a Radiometer PHM 4c pH meter and a glass electrode. All values of pH were determined at the temperature appropriate to the particular experiment through the use of a thermostated water bath with which the solutions were equilibrated prior to and during the measurement.

Results

First-, second-, and corrected second-order rate constants (see Experimental Section) for the attack of semicarbazide on *p*-hydroxybenzaldehyde in aqueous solution, ionic strength 0.50, at three values of pH at each of three temperatures are collected in Table I. The dependence of the corrected second-order rate constants on the concentration of the conjugate acid of semicarbazide is shown graphically in Figure 1. The slopes and intercepts of these plots were obtained as described in the Experimental Section. From the slopes at 25 and 35°, values of the catalytic rate constant for the conjugate acid of semicarbazide, k_{SCH^+}, were evaluated. The intercepts of plots in Figure 1
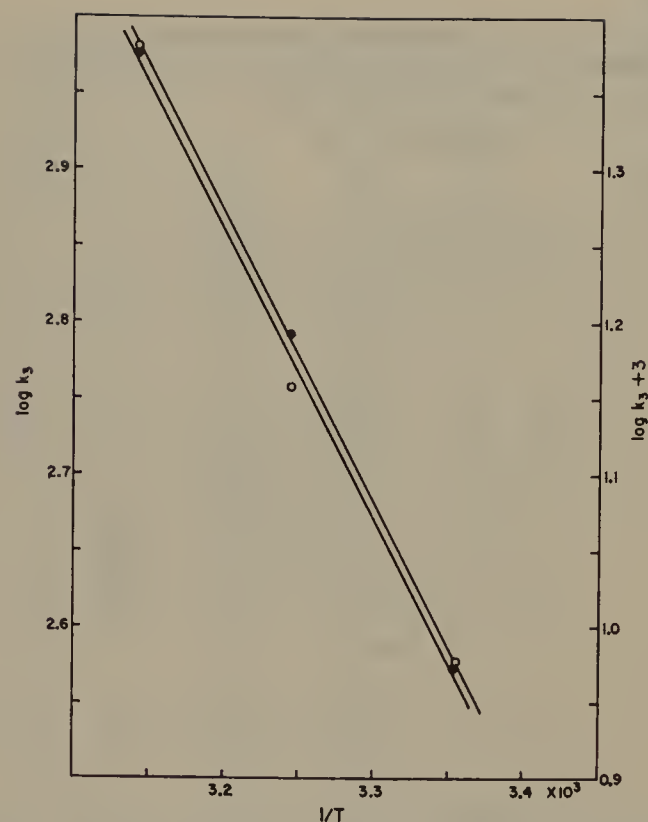
Figure 3. Arrhenius plots for *p*-hydroxybenzaldehyde semicarbazone formation catalyzed by the hydrated proton, ● and left ordinate, and by solvent, O and right ordinate. The points in this plot are taken from the data of Table III.

have been plotted against the activity of the hydrated proton in Figure 2. The slopes of these plots are equal to the catalytic constants for the hydrated proton, k_{H^+}, and the intercepts, when divided by the molar concentration of water, 55, yield the catalytic constants for water, k_0.

First- and second-order rate constants for the attack of semicarbazide on *p*-hydroxybenzaldehyde under similar conditions are presented as a function of formic acid concentration at two values of pH and at each of three temperatures in Table II. The third-order rate constants for the formic acid catalyzed reactions were evaluated from a least-squares analysis of a plot of second-order rate constants against the concentration of undissociated formic acid for each set of data. Values for each temperature were obtained by averaging the third-order rate constants for the two values of pH at that temperature.

In Table III, the third-order rate constants for catalysis of this reaction by solvent, by the hydrated proton, by the conjugate acid of semicarbazide, and by formic acid are collected and presented as a function of temperature. All values at 25° are in excellent agreement with those previously obtained for these reactions except that for the reaction catalyzed by the hydrated proton for which a value of 567 M^{-2} sec^{-1} was previously reported.[3d]

Enthalpies of activation have been derived from least-squares analysis of Arrhenius plots constructed from data of Table III and the relationship $\Delta H^\ddagger = E_a - RT$. Values are tabulated in Table IV. The Arrhenius plots for k_{H^+} and k_0 are shown in Figure 3. These plots are satisfactory though not particularly precise. That for catalysis by formic acid, k_{HCOOH}, is not so satisfactory and less reliance may be placed in the derived values. The complicated analysis required to derive the third-order rate constants for the water and

Table I. First- and Second-Order Rate Constants for Attack of Semicarbazide on *p*-Hydroxybenzaldehyde in 3.3% Aqueous Ethanol as a Function of Temperature

Temp, °C	pH	Semicarbazide, M Total	Semicarbazide, M Free base	k_{obsd}, sec^{-1}	k_2, M^{-1} sec^{-1}	$k_2(cor)$,[a] M^{-1} sec^{-1}
25	4.20	0.008	0.00611	0.000608	0.0995	0.101
	4.15	0.016	0.01209	0.001814	0.1501	0.150
	4.15	0.020	0.01520	0.002509	0.1650	0.165
	4.15	0.024	0.01824	0.003372	0.1849	0.185
	4.55	0.008	0.00709	0.000528	0.0745	0.075
	4.60	0.012	0.01076	0.000742	0.0691	0.071
	4.56	0.016	0.01422	0.001195	0.0840	0.084
	4.53	0.020	0.01762	0.001783	0.1012	0.100
	4.54	0.024	0.02119	0.002384	0.1125	0.112
	3.76	0.008	0.00450	0.00075	0.1667	0.167
	3.76	0.012	0.00672	0.00139	0.2068	0.207
	3.76	0.016	0.00903	0.00209	0.2308	0.231
	3.76	0.020	0.01126	0.00284	0.2520	0.252
	3.77	0.024	0.01365	0.00381	0.2793	0.281
35	4.14	0.012	0.00931	0.00162	0.174	0.174
	4.14	0.016	0.01242	0.00231	0.186	0.186
	4.12	0.020	0.01536	0.00333	0.217	0.214
	4.15	0.024	0.01872	0.00399	0.219	0.220
	4.49	0.008	0.00709	0.00081	0.114	0.114
	4.56	0.012	0.01082	0.00111	0.100	0.104
	4.59	0.016	0.01441	0.00143	0.099	0.105
	4.45	0.020	0.01794	0.00284	0.158	0.156
	4.51	0.024	0.02139	0.00302	0.141	0.142
	3.74	0.008	0.00451	0.00116	0.258	0.257
	3.73	0.012	0.00672	0.00189	0.282	0.282
	3.73	0.020	0.01126	0.00369	0.328	0.328
	3.73	0.024	0.01365	0.00521	0.381	0.381
45	4.01	0.008	0.00595	0.00165	0.277	0.257
	4.10	0.012	0.00935	0.00215	0.230	0.230
	4.10	0.016	0.01248	0.00311	0.249	0.249
	4.18	0.020	0.0162	0.00359	0.221	0.235
	4.14	0.024	0.0191	0.00505	0.264	0.271
	4.44	0.008	0.00712	0.00106	0.149	0.149
	4.46	0.012	0.01078	0.00222	0.206	0.208
	4.44	0.016	0.01425	0.00252	0.177	0.177
	4.36	0.020	0.01735	0.00396	0.228	0.219
	4.46	0.024	0.02139	0.00383	0.179	0.181
	3.69	0.008	0.00448	0.00195	0.435	0.434
	3.70	0.012	0.00672	0.00303	0.451	0.451
	3.71	0.016	0.00897	0.00419	0.467	0.468
	3.70	0.024	0.01342	0.00829	0.617	0.617

[a] Second-order rate constants corrected to constant pH as described in the text. The following values of pH have been chosen for the individual sets of data reading from the top down: 4.15, 4.55, 3.76, 4.14, 4.49, 3.73, 4.10, 4.44, and 3.70.

Table II. Formic Acid Catalysis of the Attack of Semicarbazide on *p*-Hydroxybenzaldehyde in 3.3% Aqueous Ethanol as a Function of Temperature

Temp, °C	pH	Formic acid,[a] M	Semicarbazide,[b] M	k_{obsd}, sec^{-1}	k_2, M^{-1} sec^{-1}
25	3.85	0.004428	0.00613	0.00123	0.200
	3.87	0.008624	0.00624	0.00138	0.221
	3.87	0.017248	0.00624	0.00156	0.250
	3.85	0.022140	0.00613	0.00208	0.339
	3.87	0.025872	0.00624	0.00231	0.371
	3.45	0.013300	0.00387	0.00172	0.445
	3.48	0.02604	0.00403	0.00194	0.502
	3.45	0.03330	0.00387	0.00250	0.646
	3.45	0.03996	0.00387	0.00270	0.699
35	3.91	0.00409	0.00645	0.00195	0.302
	3.87	0.01295	0.00624	0.00291	0.466
	3.95	0.02073	0.00666	0.00358	0.537
	3.90	0.02488	0.00640	0.00392	0.613
	3.52	0.00635	0.00454	0.00231	0.508
	3.51	0.01280	0.00448	0.00270	0.602
	3.48	0.01967	0.00431	0.00335	0.777
	3.44	0.02706	0.00409	0.00391	0.955
	3.50	0.03226	0.00442	0.00462	1.043
45	3.80	0.00489	0.00640	0.00195	0.304
	3.78	0.00998	0.00627	0.00286	0.457
	3.75	0.01540	0.00613	0.00356	0.580
	3.74	0.02088	0.00605	0.00375	0.621
	3.73	0.02625	0.00602	0.00490	0.806
	3.49	0.00658	0.00466	0.00264	0.570
	3.46	0.01351	0.00446	0.00393	0.881
	3.45	0.02037	0.00443	0.00424	0.956
	3.43	0.02758	0.00433	0.00452	1.036
	3.43	0.03440	0.00431	0.00522	1.211
	3.42	0.04157	0.00426	0.00677	1.588

[a] Of the undissociated acid. [b] Of the free base.

Table III. Temperature Dependence of Catalytic Constants for Attack of Semicarbazide on *p*-Hydroxybenzaldehyde in 3.3% Aqueous Ethanol

Temp, °C	k_{H^+}, M^{-2} sec^{-1}	k_{H_2O}, M^{-2} sec^{-1}	k_{HCOOH}, M^{-2} sec^{-1}	k_{SCH^+}, M^{-2} sec^{-1}
298.17	375	0.00095	8.75	16
308.18	620	0.00144	18.75	17
318.18	947	0.00240	23.50	..

Table IV. Activation Parameters for Catalysis of the Attack of Semicarbazide on *p*-Hydroxybenzaldehyde

Catalyst	$\Delta G^{\ddagger}$, kcal/mole	$\Delta H^{\ddagger}$, kcal/mole	$\Delta S^{\ddagger}$, eu
Hydrated proton	13.7	8.8	−16.5
Water	21.7	8.7	−43.4
Formic acid	16.2	8.7	−25.1
Protonated semicarbazide	15.9	<8	<−26

hydrated proton reactions, due to the complexity of the rate laws, makes measurements of these quantities to an accuracy greater than ±10% difficult. Consequently, it is possible that the derived enthalpies of activation for these reactions are in error by as much as 2 kcal/mole. Insufficient data were collected for evaluation of activation parameters for the semicarbazide cation promoted reaction but, judging from the data at just two temperatures, it seems reasonable to conclude that $\Delta H^{\ddagger}$ for this reaction is less than that for the formic acid catalyzed case. Since the values of $\Delta G^{\ddagger}$ are about the same for these two cases, it follows that $\Delta S^{\ddagger}$ must be more negative for the reaction catalyzed by the conjugate acid of semicarbazide. The most striking aspect of these data is that the enthalpies of activation are reasonably independent of the nature of the catalyst.

Equilibrium constants for the addition of semicarbazide to *p*-chlorobenzaldehyde to form the carbinol-

amine have been evaluated at three temperatures from the change in optical density at 259 mμ as a function of the concentration of semicarbazide as detailed in the Experimental Section. The data are presented in Table V and plots of $(OD_0 - OD)/(RNH_2)$ against OD are shown in Figure 4. Equilibrium constants were evaluated from the least-squares slopes of these plots. These equilibrium constants together with the derived thermodynamic parameters are collected in Table VI.

Table V. Data for Evaluation of Equilibrium Constants for Addition of Semicarbazide to p-Chlorobenzaldehyde at Various Temperatures[a]

Semicarb-azide, M	Optical density[b] at temperatures, °K		
	298.17	308.07	318.22
0.00	0.774	0.539	0.630
0.06			0.566
0.12		0.419	0.515
0.18	0.515	0.381	0.475
0.24	0.470	0.350	0.445
0.30	0.433	0.324	0.423
0.36	0.404	0.305	
0.42	0.374	0.295	0.382
0.48	0.355		

[a] Reaction mixtures contain 0.01 M phosphate buffer, pH 7.9, ionic strength 0.50. [b] 259 mμ.

Table VI. Equilibrium Constants and Thermodynamic Parameters for Carbinolamine Formation from p-Chlorobenzaldehyde and Semicarbazide in 3.3% Aqueous Ethanol

Temp, °K	K,[a] M^{-1}	$\Delta G°$, kcal/mole	$\Delta H°$, kcal/mole	$\Delta S°$, eu
298.17	3.48	−0.74	−2.3	−5.4
308.07	3.20			
318.22	2.72			

[a] K = (carbinolamine)/(aldehyde)(amine).

Table VII. Rate Constants for p-Chlorobenzaldehyde Semicarbazone Formation in the Region of Rate-Determining Carbinolamine Dehydration as a Function of Temperature

Temp, °K	Semicarba-zide, M	pH	$k_{obsd} \times 10^3$, sec^{-1}	k_3[a] $\times 10^{-5}$, M^{-2} sec^{-1}
298.25	0.01	6.18	0.915	1.413
	0.02	6.20	1.747	1.470
	0.03	6.20	2.438	1.455
	0.04	6.19	3.652	1.592
	0.01	6.33	0.612	1.356
	0.02	6.30	1.396	1.489
	0.03	6.34	1.737	1.417
	0.04	6.29	2.84	1.578
	0.01	6.58	0.371	1.458
	0.02	6.63	0.596	1.359
	0.03	6.60	0.989	1.450
			Av	1.458
308.17	0.01	6.15	1.261	1.838
	0.02	6.18	2.087	1.681
	0.03	6.16	2.772	1.843
	0.04	6.20	4.05	1.805
	0.01	6.37	0.760	1.859
	0.02	6.38	1.398	1.773
	0.03	6.39	2.098	1.985
	0.04	6.37	2.678	1.760
	0.04	6.72	1.346	1.967
	0.06	6.70	2.044	2.044
	0.08	6.70	2.612	2.055
			Av	1.883
318.14	0.01	6.24	1.187	2.134
	0.02	6.25	2.344	2.197
	0.03	6.26	3.227	2.116
	0.04	6.25	4.320	2.128
	0.01	6.30	1.175	2.407
	0.02	6.31	1.998	2.132
	0.03	6.32	2.737	2.051
	0.04	6.30	4.081	2.276
	0.02	6.70	0.911	2.352
	0.04	6.69	1.620	2.197
	0.06	6.70	2.411	2.312
			Av	2.209

[a] $k_3 = [k_{obsd}/(H^+)(RNH_2)][1 + K(RNH_2)]$ in which (RNH_2) is the concentration of semicarbazide free base and K is the equilibrium constant for formation of the carbinolamine.
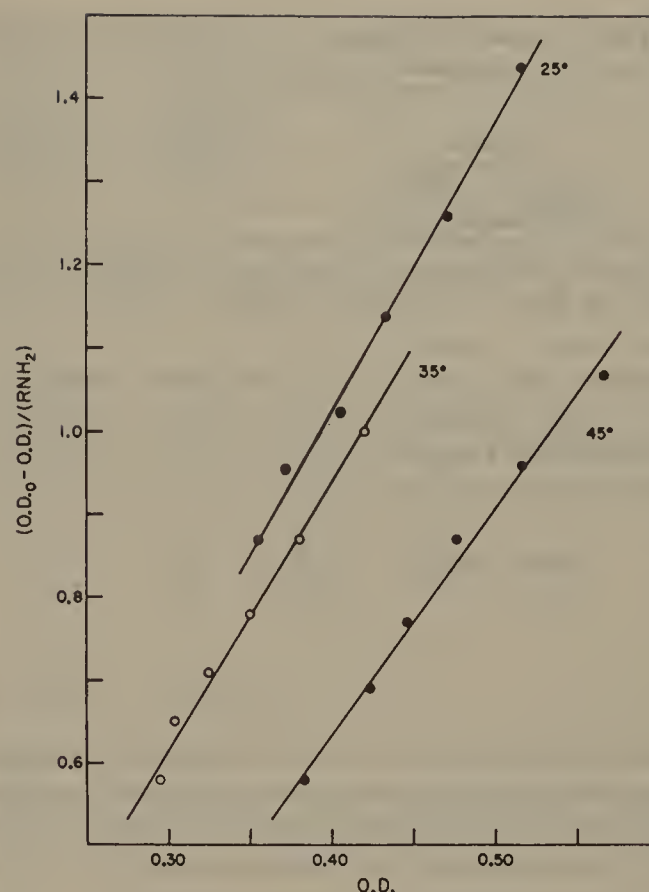
Figure 4. Change in optical density at 259 mμ divided by the concentration of semicarbazide free base plotted against the observed optical density at this wavelength for the addition of increasing concentrations of semicarbazide to p-chlorobenzaldehyde at pH 7.9. The slopes of these lines are equal to the equilibrium constants for carbinolamine formation.

The value for 25° is in agreement with a value of 4.14 M^{-1} measured in 25% ethanol and at ionic strength 0.32.[3b] The $\Delta H°$ for carbinolamine formation is considered to be accurate to within ± 1.5 kcal/mole.

In Table VII, first- and third-order rate constants for formation of p-chlorobenzaldehyde semicarbazone under conditions of rate-determining carbinolamine dehydration at three temperatures are collected. The value at 25° is in excellent agreement with a value previously determined at this temperature and in 25% ethanol, ionic strength 0.32.[3b] For each temperature, data were collected for three or four concentrations of semicarbazide at each of three values of pH. Dilute solutions of semicarbazide were employed throughout so that only a small fraction of the carbonyl compound was converted to the carbinolamine in a preequilibrium reaction. Small corrections for the conversion that did occur were made employing the measured equilibrium constants at each of the temperatures as indicated in Table VI. Activation parameters for the over-all third-order reaction were calculated from these data and are collected in Table VIII. Enthalpies of activation are considered accurate to within ± 1.5 kcal/mole.

Knowledge of the activation parameters for the over-all third-order reaction in the region of rate-determining p-chlorobenzaldehyde carbinolamine dehydration and of the standard enthalpy and entropy changes for formation of the p-chlorobenzaldehyde carbinolamine permits a calculation of the activation parameters for the decomposition of the carbinolamine. This reaction is second-order: first-order in carbinolamine and first-order in protons. The second-order rate constant is given by $k_2 = k_3/K$ (eq 4). Hence, the activation

Table VIII. Activation Parameters Associated with Semicarbazone Formation under Conditions of Rate-Determining Carbinolamine Dehydration[a]

Substrate	$\Delta G_3^{\ddagger}$, kcal/mole	$\Delta H_3^{\ddagger}$, kcal/mole	$\Delta S_3^{\ddagger}$, eu	$\Delta G_2^{\ddagger}$, kcal/mole	$\Delta H_2^{\ddagger}$, kcal/mole	$\Delta S_2^{\ddagger}$, eu
p-Chlorobenzaldehyde	10.45	3.9	−22	11.19	6.2	−16.6
p-Nitrobenzaldehyde	...	...	...	12.15	8.9	−10.7

[a] Parameters with the subscript 3 were calculated from over-all third-order rate constants in the region of rate-determining carbinolamine dehydration; those with a subscript 2 were calculated from second-order rate constants for dehydration of the carbinolamine.

parameters associated with k_2 are given by $\Delta H_2^{\ddagger} = \Delta H_3^{\ddagger} - \Delta H^{\circ}$ and $\Delta S_2^{\ddagger} = \Delta S_3^{\ddagger} - \Delta S^{\circ}$. These have been calculated from the data of Tables VI and VII and are included in Table VIII.

$$\text{>O} + \text{RNH}_2 \underset{K}{\rightleftharpoons} \overset{\text{H}}{\underset{\text{OH}}{\text{--N--R}}} \xrightarrow[\text{(H}^+)]{k_2}$$

$$\text{>N--R} + \text{H}_2\text{O} \quad (4)$$
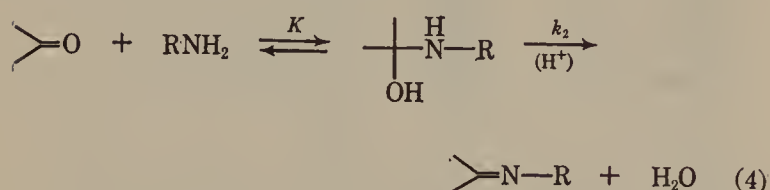
First- and second-order rate constants for formation of p-nitrobenzaldehyde semicarbazone under conditions of rate-determining carbinolamine dehydration and at three temperatures are collected in Table IX. These

Table IX. Rate Constants for p-Nitrobenzaldehyde Semicarbazone Formation under Conditions of Rate-Determining Carbinolamine Dehydration as a Function of Temperature in 3.3% Aqueous Ethanol

Temp, °K	Semi-carbazide, M	pH	$k_{obsd} \times 10^4$, sec^{-1}	α^a	$k_2,^b$ M^{-1} sec^{-1}
298.74	0.3	6.89	0.780	0.92	6.59×10^3
	0.3	7.43	0.252	0.92	7.36×10^3
	0.4	6.90	0.785	0.94	6.63×10^3
	0.4	7.44	0.238	0.94	7.02×10^3
				Av	6.90×10^3
308.04	0.3	6.88	1.28	0.92	1.05×10^4
	0.3	7.45	0.378	0.92	1.15×10^4
	0.4	6.92	1.24	0.94	1.10×10^4
	0.4	7.45	0.437	0.94	1.33×10^4
				Av	1.16×10^4
317.74	0.3	6.89	1.88	0.92	1.58×10^4
	0.3	7.11	1.26	0.92	1.77×10^4
	0.3	7.24	1.04	0.92	1.97×10^4
	0.4	7.01	1.57	0.94	1.72×10^4
	0.4	7.31	0.93	0.94	2.02×10^4
				Av	1.81×10^4

[a] The fraction of aldehyde present as the carbinolamine. [b] $k_2 = k_{obsd}/(\text{H}^+)\alpha$.

experiments were run under conditions in which more than 90% of the aldehyde was converted to the carbinolamine in a preequilibrium reaction judging from the equilibrium constants for this reaction previously published.[3b] This equilibrium constant was employed to correct the second-order rate constants to those that would have been obtained had complete conversion to the carbinolamine been achieved (see Experimental Section). At each temperature, at least four separate runs were performed. From the average values for the second-order rate constants at each temperature, activation parameters were calculated. These are included

in Table VIII. The second-order rate constant obtained at 25° is in accord with a previously reported value.[3b]

Discussion

Semicarbazone formation from benzaldehydes proceeds via the formation of a carbinolamine intermediate as indicated in eq 4. Under acidic conditions, the formation of the carbinolamine is the rate-determining step while in neutral or alkaline solutions, acid-catalyzed dehydration of the carbinolamine is rate determining.[3a,b,d] Carbinolamine formation from aromatic aldehydes and semicarbazide is markedly subject to general acid catalysis while decomposition of such species is rather insensitive to catalysis of this type.[3a,b,d]

Activation parameters for the attack of semicarbazide on p-hydroxybenzaldehyde, collected in Table IV, suggest the tentative generalization that the relative efficiencies of different catalysts for this reaction reflect principally changes in the entropy of activation. Thus, within the error of experimental measurement, enthalpies of activation for catalysis by the hydrated proton, water, and formic acid are equal while the entropies of activation become progressively more negative as the efficiency of the catalyst decreases. The force of this generalization is weakened by two factors. First, the catalysts are structurally dissimilar and, hence, the activation parameters may contain quite variant contributions from solvation factors and the like. Second, it is possible that the catalytic mechanisms may differ from catalyst to catalyst; earlier work does suggest, however, that water and the hydrated proton, like formic acid, act as general acid catalysts.[3c,d] Ideally, one should evaluate activation parameters for structurally similar general acid catalysts such as a series of substituted acetic acids. However, in systems as complicated as this one, evaluation of such parameters for these catalysts with sufficient accuracy to permit meaningful conclusions to be drawn would prove a challenging task. Some agreement has been reached, on the basis of different considerations, that the transition state for general acid catalyzed carbonyl addition reactions involves hydrogen-bond formation between the acid catalyst and the carbonyl oxygen atom.[3d,13,14] In terms of such a transition state, it would seem likely that increasing the strength of the acid catalyst should reduce the enthalpy of activation. However, it is well known that differences in the ionization of carboxylic acids and phenols show up largely in the entropy terms; perhaps the current observations are, in part, a reflection of similar behavior for reactions involving only partial proton transfer.

(13) C. G. Swain and J. C. Worosz, *Tetrahedron Letters*, 3199 (1965).
(14) C. G. Swain, D. A. Kuhn, and R. L. Schowen, *J. Am. Chem. Soc.*, 87, 1553 (1965).

The similarity of enthalpies of activation for general acid catalyzed and solvent-catalyzed attack of semicarbazide on p-hydroxybenzaldehyde is in marked contrast to behavior noted in reactions involving nucleophilic attack at acyl carbon. A particularly nice example has been discovered by Bruice and Benkovic for the reaction of hydrazine with phenyl acetates.[15] In this system, enthalpies of activation decrease markedly from the solvent-catalyzed to the general base catalyzed to the general acid catalyzed reaction. At the same time, the entropies of activation become increasingly negative so that the over-all rate constants do not vary greatly as a function of the type of catalysis involved. Similar results have been obtained for the aminolysis of thiol esters[16] and alkylaminolysis of phenyl acetate.[17] This clear difference in behavior may reflect different mechanisms of catalysis, distinct roles for solvent in the two types of reaction, or simply the difference in charge type of the catalyst.

The thermodynamic quantities for the addition of semicarbazide to p-chlorobenzaldehyde are similar to those for the addition of water to monochloroacetone.[18] The hydration of more reaction carbonyl compounds exhibits substantially more negative values of $\Delta H°$ and $\Delta S°$[18] as does the addition of cyanide ion to acetone in water.[19] The modest loss of entropy in carbinolamine formation presumably reflects the loss of translational freedom of the molecule of amine.

A number of early determinations of activation parameters for carbonyl addition reactions, including oxime formation,[7,8,10] semicarbazone formation,[5,6,9] and thiosemicarbazone formation,[9] were carried out under conditions in which one would expect carbinolamine dehydration to be the rate-determining step. Typically, small values for the enthalpies of activation and very large negative values for the entropies of activation were observed. These results are in accord with those noted here (Table VIII). Appreciation of this point requires the observation that most previous activation parameters were calculated from second-order, pH-dependent rate constants while we have made such calculations on the basis of third-order, pH-independent rate constants. If we recalculate our values on the basis of second-order rate constants at, for example, pH 7, we obtain a value of $\Delta S^{\ddagger}$ near -54 eu, a value similar to those previously published. Recent studies of activation parameters for nitrone formation in a region of acid catalysis have revealed values which are similar to those obtained in this study.[11] However, the conclusion of these workers that carbinolamine formation is the rate-determining step in this region must be abandoned both in light of what has been generally established about the kinetics and mechanism for carbonyl addition reactions[4] and in light of recent studies of nitrone formation by Reimann and Jencks.[3i] The activation parameters obtained are almost certainly those for acid-catalyzed, rate-determining carbinolamine dehydration.

Values of entropies of activation for acid-catalyzed carbinolamine decomposition (not those for the over-all reaction in the region of rate-determining carbinolamine dehydration which are discussed above) near -11 to -16 eu as indicated in Table VIII are surprising. These reactions are certainly unimolecular decompositions of the carbinolamine conjugate acids. Nucleophilic attack of solvent on the carbinolamines would, in fact, simply regenerate the same carbinolamine. Unimolecular acid-catalyzed reactions usually exhibit entropies of activation near zero, although exceptions are known.[20] This reaction must be added to those known to exhibit anomalous entropies of activation. Perhaps the substantial negative entropy of activation reflects loss of rotational degrees of freedom associated with the developing carbon–nitrogen double bond.

(15) T. C. Bruice and S. J. Benkovic, J. Am. Chem. Soc., 86, 418 (1964).
(16) L. R. Fedor and T. C. Bruice, ibid., 86, 4117 (1964).
(17) W. P. Jencks and M. Gilchrist, ibid., 88, 104 (1966).
(18) R. P. Bell and A. O. McDougall, Trans. Faraday Soc., 56, 1281 (1960).
(19) T. Stewart and B. Fontana, J. Am. Chem. Soc., 62, 3281 (1940).

(20) L. L. Schaleger and F. A. Long, Advan. Phys. Org. Chem., 1, 1 (1963).

[3.2]Metacyclophanes. Conformational Studies

Rodger W. Griffin Jr.,[1a] and Robert A. Coburn[1b]

Contribution from the Department of Chemistry, Harvard University, Cambridge, Massachusetts 02138. Received March 4, 1967

Abstract: The energy barriers to ring inversion of the 11-membered aromatic–aliphatic rings in a number of 2-substituted [3.2]metacyclophanes were determined from the temperature dependence of their proton magnetic resonance spectra. The energy barriers to ring inversion were found to be dependent upon the steric nature of the 2-substituent and lie between 15.8 and 19.1 kcal/mole in the temperature range 60–120°. Bulky 2 substituents were found to produce conformational changes in 2-monosubstituted derivatives with respect to 2,2-symmetrically disubstituted derivatives. A half-life at 0° of 2.4 sec for the stable conformers of [3.2]metacyclophane-2-carboxylic acid is predicted from the activation energy parameters for ring inversion obtained from the nmr data. In comparison, [2.2]metacyclophane is estimated to have a barrier to ring inversion of greater than 26–28 kcal/mole.

The unique geometry of the [2.2]metacyclophane system which results in the crowding of two aromatic rings[2] leads to a number of interesting physical and chemical properties. These include transannular effects and reactions,[2b] unusual aspects in the proton magnetic resonance spectrum,[3] and strain and rigidity in the ten-membered aromatic–aliphatic ring resulting in a very unreactive benzylic position.[4]

These interesting properties have prompted the synthesis of [3.2]metacyclophanes and the study of their physical and chemical properties. We report here the results of conformational studies of a number of 2-substituted [3.2]metacyclophanes.

Method

The compounds examined were obtained from diethyl [3.2]metacyclophane-2,2-dicarboxylate whose synthesis has been reported earlier.[5] The 9,17-proton magnetic resonance frequency in [3.2]metacyclophanes exhibits a diamagnetic shift of *ca.* 2.1 ppm relative to that of the other methine protons. In symmetrically 2,2-disubstituted derivatives this signal appears as a singlet broadened slightly by weak coupling with the *meta* and *para* protons. However, in 2-monosubstituted [3.2]metacyclophanes the 9,17 protons exhibit different chemical shifts. A number of 2-monosubstituted derivatives were synthesized from diethyl [3.2]metacyclophane-2,2-di-

carboxylate in order to determine the origin of the chemical shift difference.

Ring inversion in 2-monosubstituted [3.2]metacyclophanes exchanges the 9 and 17 positions with respect to the substituent. The temperature dependence of the line positions of the 9,17-proton magnetic resonance was used to determine ring inversion rates in the range of "intermediate exchange rates."[6,7] The method employed was that of Gutowsky and Holm[8a] in which signals from two noninteracting protons of different chemical shift coalesce to a single line by the exchange of their environments; $k_t = \pi \sqrt{(\nu^2 - \Delta_t^2)/2}$. The rate of exchange at temperature T_i can be estimated from the frequency separation at the temperature (Δ_t) and the frequency separation under conditions of no exchange (ν). The separation frequency under conditions of no appreciable exchange was obtained by progressively lowering the temperature until no further increase in separation frequency was observed. A correction for overlap of components was unnecessary due to the large frequency separations relative to the observed line widths. The estimated systematic error in this method was found to be less than the experimental error for this system.[8b] The weak coupling of the 9,17 protons to the remaining aromatic protons hindered application of the line shape and line broadening techniques to obtain additional kinetic data.

Results

Listed in Table I are the maximum frequency separations of the 9,17-proton magnetic resonance signals of a number of 2-monosubstituted [3.2]metacyclophanes, obtained by progressively lowering the sample temperature. By raising the temperature these frequency separations fell to zero, in all cases, as ring inversion became rapid. Regardless of the exact origin of these chemical shift differences, the separation frequencies provided kinetic data for the ring inversion. Although the broad unresolved bridging methylene protons'

(2) (a) C. J. Brown, *J. Chem. Soc.*, 3278 (1953); (b) N. L. Allinger, M. A. DaRooge, and R. B. Hermann, *J. Am. Chem. Soc.*, 83, 1974 (1961). The authors of these papers explain the distortions reported in this molecule to be due to repulsions between benzenoid rings. However, it seems anomalous that four bond angles should be distorted by 15° while four others also available for the relief of strain suffer no deformation whatever.

(3) D. J. Wilson, V. Boekelheide, and R. W. Griffin, Jr., *ibid.*, 82, 6302 (1960).

(4) R. W. Griffin, Jr., *Chem. Rev.*, 63, 45 (1963).

(5) R. W. Griffin, Jr., and R. A. Coburn, *Tetrahedron Letters*, 2571 (1964).

(6) J. A. Pople, W. G. Schneider, and H. J. Bernstein, "High-Resolution Nuclear Magnetic Resonance," McGraw-Hill Book Co., Inc., New York, N. Y., p 218.

(7) A number of examples of the application of this method are available: (a) K. G. Untch and R. J. Kurland, *J. Am. Chem. Soc.*, 85, 346 (1963); (b) P. Radlick and S. Winstein, *ibid.*, 85, 344 (1963); (c) F. R. Jensen, D. S. Noyce, C. H. Sederholm, and A. J. Berlin, *ibid.*, 84, 386 (1962).

(8) (a) H. S. Gutowsky and C. H. Holm, *J. Chem. Phys.*, 25, 1228 (1956); (b) A. Allerhand, H. S. Gutowsky, J. Jonas, and R. A. Meinzer, *J. Am. Chem. Soc.*, 88, 3185 (1966).

resonance signals became greatly simplified at higher temperature, the poor definition of the spectra at low temperature limited their usefulness in providing kinetic data.

Table I. Frequency Separations between 9- and 17-Proton Magnetic Resonance Signals in Various 2-Monosubstituted [3.2]Metacyclophanes

Compd	2-Substituent	ν, Hz
1	CN	4.5
2	CO_2H	19.8
3	CO_2CH_3	23.0
4	COCl	25
5	$CONH_2$	35
6	$CONEt_2$	35
7	CON-i-Pr$_2$	37
8	$C(CH_3)_2OH$	70
9	$C(Ph)_2OH$	77

Figure 1 represents plots of the kinetic data for methyl [3.2]metacyclophane-2-carboxylate and [3.2]-metacyclophane-2-carboxylic acid. The coalesence temperatures for the ester and acid were 59.3 and 53.9°, respectively. Rates of ring inversion were determined in the temperature range of 40–60°. Table II contains the activation energy parameters for the ring inversion of ester 3 and acid 2.[9] The energy barriers to ring inversion in alcohols 8 and 9 were determined from the rate of inversion at the temperature which their 9,17-proton signals coalesce using the absolute rate theory.[10,11]

Table II. Energies of Activation for Ring Inversion in a Number of 2-Monosubstituted [3.2]Metacyclophanes

Compd	2-Substituent	$\Delta H^{\ddagger}$, kcal/mole	$\Delta S^{\ddagger}$, eu	$\Delta F^{\ddagger}_{60°}$, kcal/mole
2	CO_2H	15.81 ± 0.2	−2.9	16.8 ± 0.2
3	CO_2CH_3	16.06 ± 0.2	−2.4	16.8 ± 0.2
8	$C(CH_3)_2OH$			16.2 ± 0.3
9	$C(Ph)_2OH$			15.7 ± 0.3

Attempts were made to resolve [3.2]metacyclophane-2-carboxylic acid using various optically active amine bases (brucine, strychnine, cinchonine, and d-α-methylbenzylamine) in a number of solvent systems. No evidence of a successful resolution could be obtained. The stable conformers of [3.2]metacyclophane-2-carboxylic acid were predicted to have a mean half-life at 0° of 2.4 sec based upon the activation energy parameters derived from the nmr data.

2-Benzhydrylidene[3.2]metacyclophane was prepared from methyl [3.2]metacyclophane-2-carboxylate and was

(9) F. W. Cagle, Jr., and H. Eyring, *J. Am. Chem. Soc.*, 73, 5628 (1951); a least-squares treatment was applied. Sample calculations show that the probable error in $\Delta H^{\ddagger}$ which is introduced by the uncertainty in ν exceeds, by an order of magnitude, that which is introduced by the uncertainty in T (±1°) or Δ (±0.2 Hz).

(10) The values of $\Delta F^{\ddagger}$ for compounds 8 and 9 could not be determined in the same manner as those for compounds 2 and 3. In one case solubility problems and in the other case uncertainties due to line width precluded a determination of ν with sufficient accuracy to justify application of the former method. Small errors in ν were found to produce gross errors in $\Delta F^{\ddagger}$.

(11) S. Glasstone, K. J. Laidler, and H. Eyring, "The Theory of Rate Processes," McGraw-Hill Book Co., Inc., New York, N. Y., 1941, p 195.
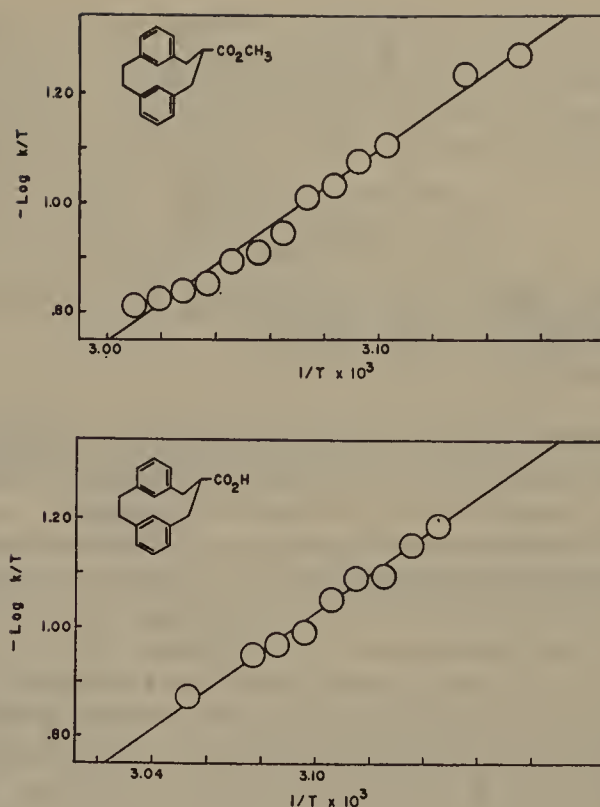
Figure 1. Plots of ring inversion rate data for methyl [3.2]meta-cyclophane-2-carboxylate and [3.2]metacyclophane-2-carboxylic acid.

found to exhibit bridging methylene proton resonance frequencies sufficiently separated to allow observation of the simultaneous collapse of the AB (three-membered bridge) and A_2B_2[12] (two-membered bridge) systems upon heating. Although not strictly an AX system, the AB system (ν = 39 cps, J = 10 cps) provided a good estimate of the rate of ring inversion at its coalescence temperature. This temperature was, within experimental error, the same as the coalescence temperature for the A_2B_2 system. The energy barrier to ring inversion,[11] 17.3 ± 0.3 kcal/mole at 72°, was expected to be less than that for symmetrically 2,2-disubstituted [3.2]-metacyclophanes due to relaxation in strain upon substitution of a trigonally hybridized carbon atom for a tetrahedral ring member.

The nmr spectrum of [2.2]metacyclophane previously described[2] and studied in detail[13] remains unchanged over the temperature range 20–200°. This allows an estimate of the lower limit of the energy barrier to ring inversion for [2.2]metacyclophane of 26–28 kcal/mole.

Discussion

The magnitude of the chemical shift difference between the 9 and 17 protons and the remote location of the substituents indicate that this difference does not arise from an induced modification in the nature of the carbon–hydrogen bond. This difference most likely arises from a modification of the secondary diamagnetic field experienced by the 9,17 protons which results from the "induced ring current" in the benzenoid rings.[14] This

(12) Rotation about the C_{10}–C_{11} bond caused by the three-membered bridge may result in this system being more properly labeled as an ABXY system.

(13) H. S. Gutowsky and C. Juan, *J. Chem. Phys.*, 37, 120 (1962).

(14) Regardless of the origin of the anisotropic magnetic effects in benzenoid hydrocarbons arising from a ring current (see R. J. Abraham and W. W. Thomas, *J. Chem. Soc.*, 127 (1966)), or arising partially (J. A. Pople, *J. Chem. Phys.*, 41, 2559 (1964)), or totally (J. I. Musher, *ibid.*, 43, 4081 (1965)) from localized electrons, the above arguments are valid. The ring current based on calculations of C. E. Johnson and
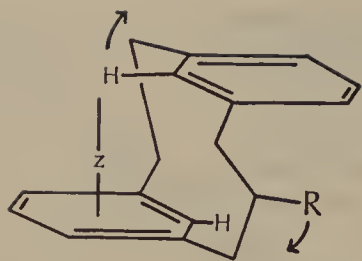
Figure 2. Effect of bulky 2-substituent on the conformation of 2-monosubstituted [3.2]metacyclophane.

diamagnetic field produces a shift of the 9,17-protons' resonance signals by *ca.* 125 Hz to higher field from the normal aromatic proton resonance frequency.

This change in the diamagnetic field effect can be brought about by a change in the 9,17-protons' positions in the induced field or by a modification of the field itself. The former situation would occur with any conformational change which moved the C_9–H and C_{17}–H bond axes out of parallel planes. This would destroy an element of symmetry in the molecule which allows the 9,17 protons in symmetrically 2,2-disubstituted [3.2]-metacyclophanes to experience identical electronic environments. The second explanation would require that the substituent modify the induced diamagnetic field of the benzenoid rings by, perhaps, an inductive field perturbation of the aromatic rings or by an anisotropic contribution of its own to the secondary magnetic field experienced by the 9,17 protons.

The results tabulated in Table I suggest that steric effects play a primary role in the origin of the frequency separations between 9,17 proton signals in 2-monosubstituted [3.2]metacyclophanes. The smallest shift difference occurs in nitrile **1** from which one would expect a large anisotropic effect (with the proper orientation). The same is true of diphenyl alcohol **9** which exhibits a frequency separation very similar to that of dimethyl alcohol **8**. These results argue against an anisotropic effect by the substituent while the magnitude of the separations, especially in the case of the alcohols, seems to be much greater than that which would arise by an inductive effect by the substituent on the benzenoid rings.

If the derivatives are classified according to the steric nature of their substituent (CX, CX_2, CX_3), the frequency separations between 9- and 17-proton signals of members within each group are similar. Furthermore, the magnitude of the frequency separation correlates with the degree of branching in the α position of the substituent.

A steric interaction between the substituent and the nearest benzenoid ring would be relieved by the substituent assuming a pseudo-equatorial position with respect to the 11-membered aromatic–aliphatic ring. Such a movement produces a change in attitude between the two benzenoid rings when torsional strain is minimized. Thus, the 9,17 protons change their positions relative to the centers of their nonbonded benzenoid rings in a dissymmetric fashion (Figure 2). Due to the large field gradient in the induced secondary diamagnetic field in the region in which the 9,17 protons are found (as evidenced by the magnitude of the observed dia-

magnetic shift), the conformational change necessary to produce even the largest of the observed frequency separations would not need to be great.[15]

One may expect a lower enthalpy of activation for ring inversion to result from any appreciable destabilization of the ground-state conformer produced by steric interactions as long as these interactions are absent in the transition state. The energy barriers to ring inversion in the two metacyclophanes **8** and **9**, containing the substituents which produce the largest conformational change, show a small (in comparison to the reliability of the data) but significant decrease. Since the enthalpies of activation for these compounds are not known, it can only be hypothesized that these lower energy barriers result from a lower enthalpy of activation caused by the steric interactions of the substituents. But the similarity of the compared systems and the expected reverse effect of any change in entropy of activation make this a reasonable assumption. This suggests that these steric interactions lead to a conformational change, in the 2-monosubstituted [3.2]metacyclophanes, which a symmetrically 2,2-disubstituted [3.2]metacyclophane would have to effect while undergoing a ring inversion. Diethyl [3.2]metacyclophane-2,2-dicarboxylate-d_4 was previously estimated to possess an energy barrier of 19.1 $\pm$ 0.5 kcal/mole at 112.4°.[5]

Conclusions

The repulsive strain between aromatic rings in [2.2]-paracyclophane has been estimated to be 16 kcal/mole,[16] although this appears to be a conservative estimate in view of the 18-kcal/mole strain energy calculated for [2.2]metacyclophane which has fewer steric interactions.[2b] This type of strain in the *cis* ring conformation **10** would be less due to the greater separation allowed between benzenoid rings. In view of the energy barriers to ring inversion for a number of [3.2]metacyclophanes (16–19 kcal/mole), **10** cannot be excluded as a possible intermediate since its standard free energy level may well be below this energy barrier. The possibility remains, however, that the activation energy necessary to achieve this *cis* conformation is higher than that required to effect the ring inversion. Lack of knowledge concerning the transition-state geometry hinders solution of this question.

10
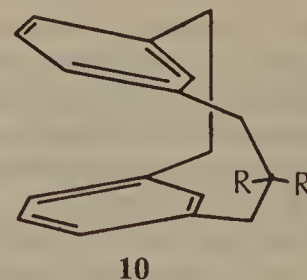
Experimental Section

Melting points were determined with a Fisher-Johns melting point apparatus and are corrected. Petroleum ether refers to Fisher Certified Reagent Grade petroleum ether (bp 40–60°). Ultraviolet spectra were recorded with a Cary spectrophotometer,

F. A. Bovey, *J. Chem. Phys.*, **29**, 1012 (1958), describe qualitatively but not quantitatively the nmr data for a number of [*m.n*]metacyclophanes: R. A. Coburn, Ph.D. Thesis, Harvard University, 1966.

(15) Calculations based on the data of Johnson and Bovey,[14] the observed diamagnetic shift, and a model incorporating some of the strain observed in [2.2]metacyclophane predict that a displacement of H_9 of only 0.2–0.5 A along the z axis (Figure 2) would be necessary to produce the observed separation frequencies.

(16) B. H. Smith, "Bridged Aromatic Compounds," Academic Press Inc., New York, N. Y., 1964, p 359.

Model 11M. Infrared spectra were obtained with a Perkin-Elmer grating spectrophotometer, Model 237. Nmr spectra were recorded in deuteriochloroform, unless otherwise noted, with a Varian A-60 nmr spectrometer equipped with a V-6040 nmr variable-temperature controller. Tetramethylsilane was used as the internal standard (0 ppm). Frequency separations were determined by locating the two signals within 0.04 Hz using the audio-frequency–side-band technique.[17]

[3.2]Metacyclophane-2-carboxylic Acid (2). Diethyl [3.2]meta-cyclophane-2,2-dicarboxylate[4] (600 mg, 1.64 mmoles) was added to a 50% aqueous potassium hydroxide solution (5 ml), and the mixture was refluxed for 4 hr. The cooled solution was diluted with water to 40 ml and washed with ether (10 ml). The aqueous solution was acidified and extracted with five 10-ml portions of ether. The combined ether extract was washed with distilled water and saturated salt solution and dried over anhydrous magnesium sulfate. Evaporation of the ether left 397 mg of [3.2]metacyclophane-2,2-dicarboxylic acid, mp 163–164° dec. This material was heated in an oil bath at 180° until the evolution of gas ceased. Recrystallization of the residue from ether–petroleum ether afforded 324 mg (74% yield) of **2** as white crystals, mp 163–164.5°, λ_{max}^{EtOH} 208 (log ϵ 4.57) and 269 mμ (log ϵ 2.59). Its infrared spectrum (KBr pellet) showed absorption at 5.93 and 3.4 μ typical of carboxylic acids. The nmr spectrum recorded at −50° showed an unresolved nine-proton multiplet at 2–3.5 ppm (bridging methylene protons), two one-proton singlets at 5.0 and 5.3 ppm (9,17 protons), a six-proton multiplet at 7.4 ppm (remaining aromatic protons), and a one-proton singlet at 11.9 ppm (carboxyl group proton).

Anal. Calcd for $C_{18}H_{18}O_2$: C, 81.17; H, 6.81. Found: C, 81.36; H, 6.85.

Attempted Resolution of [3.2]Metacyclophane-2-carboxylic Acid (2). [3.2]Metacyclophane-2-carboxylic acid was treated with 1.2 equiv of optically active amine (brucine, strychnine, or cinchonine) in ether. The resulting solution was cooled for 12 hr in a Dry Ice–acetone bath. An oil slowly formed which could not be induced to crystallize. This procedure was repeated in chloroform, tetrahydrofuran, and 1:1 benzene–ether with the same results. A crystalline salt was obtained when d-α-methylbenzylamine[18] was employed in dry acetone. However, no mutarotation or contribution to the optical activity from the cation could be detected in solutions of the recrystallized salt. A sample of **2** recovered from the salt was optically inactive.

Methyl [3.2]Metacyclophane-2-carboxylate (3). A dry, distilled solution of diazomethane in ether was slowly added to a solution of **2** (366 mg, 1.37 mmoles) in tetrahydrofuran until a yellow color persisted. Evaporation of solvent left 384 mg (100% yield) of **3** as a colorless oil which could not be induced to crystallize even after chromatography on silica gel. Its nmr spectrum taken in carbon tetrachloride was similar to that of **2** except for the absence of the one-proton singlet at 11.9 ppm and the addition of a three-proton singlet at 3.7 ppm (OCH₃). Strong carbonyl absorption at 5.78 μ is noted in the infrared.

[3.2]Metacyclophane-2-carbonyl Chloride (4). A mixture of **2** (100 mg, 0.376 mmole), benzene (1 ml), and thionyl chloride (0.25 ml) was refluxed for 1 hr. The solvent was distilled and replaced with 2 ml of dry benzene. The solvent was again distilled, and the residual oil was warmed on a steam bath under reduced pressure for 1 hr. There was obtained 110 mg of **4** as a colorless oil which was used without further purification to prepare the amides. Its nmr spectrum was very similar to that of **2** but lacked the singlet at 11.9 ppm.

[3.2]Metacyclophane-2-carboxamide (5). A solution of **4** (110 mg) in dry acetone (5 ml) was slowly added to concentrated aqueous ammonia (2 ml). After several minutes a white precipitate formed which was collected, washed with water, and recrystallized from

methanol. There resulted 50 mg of **5** as white crystals; mp 214.5–215.5°, λ^{CCl_4} 6.15 μ. Its nmr spectrum taken in deuterio-chloroform is similar to that of **4** but with a broad two-proton singlet at 5.73 ppm identified as the amide protons' signal by its absence from the spectrum taken in methanol-d₄ (with a trace of sodium methoxide added).

Anal. Calcd for $C_{18}H_{19}NO$: C, 81.48; H, 7.22; N, 5.28. Found: C, 81.79; H, 7.33; N, 5.45.

N,N-Diethyl[3.2]metacyclophane-2-carboxamide (6). A procedure identical with that described above employing diethylamine instead of ammonia was used. There resulted 157 mg (81% yield) of **6** as a colorless oil. A sample crystallized from methanol in a Dry Ice–acetone bath, but melted below room temperature; λ_{max}^{neat} 6.10 μ. The nmr spectrum was similar to that of amide **5** but lacked the amide protons' signal. A triplet at 1.15 ppm and a quartet at 3.3 ppm were assigned to the ethyl groups.

Anal. Calcd for $C_{22}H_{27}NO$: C, 82.20; H, 8.47; N, 4.36. Found: C, 81.60; H, 8.62; N, 4.25.

N,N-Diisopropyl[3.2]metacyclophane-2-carboxamide (7). A procedure identical with that described above employing diisopropyl-amine was used. These was obtained 161 mg (76% yield) of **7** as white crystals, mp 82–83.5°.

Anal. Calcd for $C_{24}H_{31}NO$: C, 82.48; H, 8.94; N, 4.01. Found: C, 82.23; H, 8.98; N, 4.13.

2-Cyano[3.2]metacyclophane (1). A mixture of **5** (50 mg, 0.188 mmole), benzene (1 ml), and thionyl chloride (0.5 ml) was refluxed for 3 hr. The solvent was evaporated and carbon tetrachloride (one drop) and petroleum ether (ten drops) were added to the resulting oil. A small amount of amide **5** precipitated and was removed by filtration. The filtrate was cooled giving white crystals which were collected and recrystallized from petroleum ether. There was obtained 28 mg (68% yield) of **1** as white needles, mp 88–89°, $\lambda_{max}^{CCl_4}$ 4.46 μ.

Anal. Calcd for $C_{18}H_{17}N$: C, 87.41; H, 6.93; N, 5.66. Found: C, 87.64; H, 6.87; N, 5.68.

Dimethyl-2-[3.2]metacyclophanemethanol (8). Ester **3** (384 mg, 1.37 mmoles) in dry ether (10 ml) was slowly added to 10 ml of 0.42 N methyllithium solution maintained at 0° in an ice bath. The mixture was stirred for 1 hr, then refluxed for 30 min. The reaction mixture was cooled and saturated ammonium chloride solution (10 ml) was added. The separated ether layer was washed with distilled water and saturated salt solution, and dried over anhydrous magnesium sulfate. Evaporation of the ether gave 379 mg (98% yield) of **8** as white crystals, mp 138–141°. A sample was recrystallized from methanol for analysis, mp 142–143.5°, $\lambda_{max}^{CCl_4}$ 2.78 μ. The nmr spectrum taken at room temperature in carbon tetrachloride showed signals at 4.62 and 5.65 ppm assigned to the 9,17 protons.

Anal. Calcd for $C_{20}H_{24}O$: C, 85.67; H, 8.63. Found: C, 85.68; H, 8.59.

Diphenyl-2-[3.2]metacyclophanemethanol (9). An analogous procedure to that described above for the preparation of **8** but employing a 3 N phenyllithium solution was used. The crude product was chromatographed on 2 g of alumina (Merck). Elution with 5% ether in benzene gave 113 mg (75% yield) of **9** as white needles, mp 146–147.5°, $\lambda_{max}^{CCl_4}$ 2.76 μ. The nmr spectrum taken at room temperature in carbon tetrachloride exhibited signals at 4.5 and 5.6 ppm assigned to the 9,17 protons.

Anal. Calcd for $C_{30}H_{28}O$: C, 89.07; H, 6.98. Found: C, 88.76; H, 6.95.

2-Benzhydrylidene[3.2]metacyclophane. A solution of **9** (117 mg, 0.29 mmole) in glacial acetic acid (2 ml) and acetic anhydride (1 ml) was refluxed for 6 hr. Evaporation of solvent at reduced pressure gave a colorless oil which crystallized on standing. Recrystallization from ether–petroleum ether gave 60 mg (50% yield) of 2-benzhydrylidene[3.2]metacyclophane as white needles, mp 172–173°, $\lambda_{max}^{CCl_4}$ 6.2 μ, λ_{max}^{EtOH} 205 (log ϵ 4.07) and 245 mμ (log ϵ 3.57). The nmr spectrum taken in carbon tetrachloride showed a two-proton singlet at 5.00 ppm assigned to the 9,17 protons.

Anal. Calcd for $C_{30}H_{26}$: C, 93.22; H, 6.78. Found: C, 93.03; H, 6.73.

(17) J. T. Arnold and M. E. Packard, *J. Chem. Phys.*, **19**, 1608 (1951).

(18) A. W. Ingersoll, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p 506.

Macro Rings. XXXV. Stereochemistry of [2.2]Paracyclophanyl Nucleus as a Neighboring Group in Solvolyses Reactions[1]

Donald J. Cram and Francis L. Harris, Jr.

Contribution No. 2042 from the Department of Chemistry of the University of California, Los Angeles, California 90024. Received April 3, 1967

Abstract: The effects of the [2.2]paracyclophanyl nucleus on the kinetics and stereochemistry of carbonium reactions at asymmetric carbon atoms α and β to the system have been examined. Hydrolysis in 9:1 dioxane–water of the trichloroacetate of the α- and β-diastereomers of 4-(1-hydroxyethyl)-[2.2]paracyclophane both gave 1:1 mixtures of the corresponding α and β alcohols, and at rates (first order) that differed by only about 10%. In methanolysis in the presence of potassium acetate, the α and β esters gave ethers whose product composition differed by only 6%. Acetolyses and formolyses of the tosylates of α- and β-4-(2-deuterio-2-hydroxypropyl)-[2.2]paracyclophane were much more stereospecific. Acetolysis at 75° of the α-tosylate gave acetate which was 97% α and 3% β, whereas the β-tosylate gave acetate which was 7% α and 93% β. In formolyses, both diastereomeric tosylates underwent reaction with greater than 99% retention of configuration. The rates of acetolysis of the two diastereomeric tosylates differed by only about 10%. The $\Delta S^{\ddagger}$ for each diastereomer was about −4 to −5 eu. These facts provide compelling evidence for intervention of a phenonium ion intermediate in the solvolyses of the latter system.

Earlier work[2] demonstrated that the [2.2]paracyclophanyl nucleus was a somewhat better neighboring group than the 2,5-dimethylphenyl group in enhancing the rates of solvolysis in both α-arylmethyl bromide and β-arylethyl tosylate systems. In particular, compounds I and II were found to be more reactive than their open-chain counterparts. In acetolysis of II, although the rates and entropies of activation indicated that aryl participated in ionization, no deuterium scrambling occurred, and therefore the intermediate phenonium ion was opened exclusively at the same position involved when the three-membered ring was closed.

I II
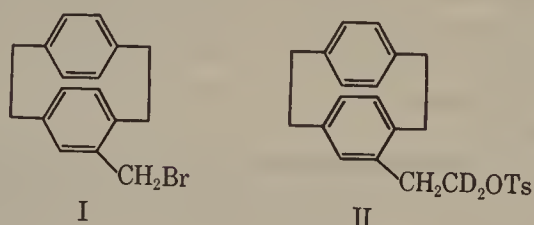
In the present work, solvolyses of the trichloroacetates of III and the tosylates of IV were examined. Both systems contain two asymmetric elements, and therefore each is composed of two racemates, III-α and III-β, and IV-α and IV-β. Thus, an examination of the structures of the products of solvolysis of the four racemates allows the stereochemical course of sub-

stitution to be determined, which in turn points to the mechanistic details of the transformations.[3]
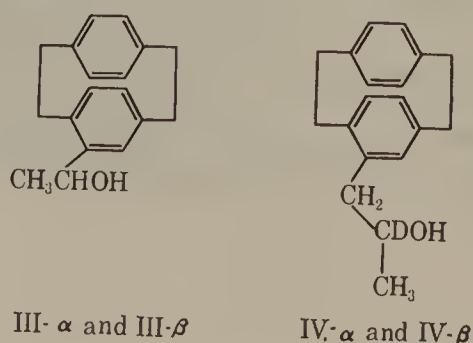
Syntheses. Racemates III-α and III-β were prepared by lithium aluminum hydride reduction of 4-acetyl[2.2]paracyclophane.[4] The two diastereomers were produced in the ratio α:β = 1.32,[5] and are experimentally designated as follows: α, mp 107–107.5°, eluted first from alumina; β, mp 117–118°, eluted second from alumina. Arguments for the relative configurational assignments are found in the Discussion. Attempts to prepare the tosylates of these alcohols failed because of the instability of the expected products. Attempted preparation of the diastereomerically pure chlorides from either alcohol III-α or III-β with anhydrous hydrogen chloride in ether or with thionyl chloride always led to inseparable mixtures of the epimeric chlorides. Consequently, the trichloroacetates of III-α and -β were prepared and employed in the solvolytic studies.[6]

The synthesis of alcohols IV was accomplished through acid V as intermediate,[7] whose synthesis was greatly improved (see Experimental Section). Ketone VI was reduced with lithium aluminum deuteride instead of the common hydride to facilitate nmr analysis of alcohols IV and their derivatives. The diastereomers were separated by silica gel chromatography of their acetates (which lent themselves to nmr analysis), reduction of which with lithium aluminum hydride led to pure IV-α and IV-β. These alcohols were produced in the ratio IV-α:IV-β = 1.26 from the ketone VI. A small amount of 1,3-asymmetric induction is visible in this ratio. These alcohols are given the following experimental designations: IV-α, mp 120–121° (acetate is eluted more rapidly from silica gel); IV-β,

III-α and III-β IV-α and IV-β

(2) D. J. Cram and L. A. Singer, *J. Am. Chem. Soc.*, 85, 1075 (1963).

(3) D. J. Cram, *ibid.*, 86, 3767 (1964).

(4) D. J. Cram and N. L. Allinger, *ibid.*, 77, 6289 (1955).

(5) This reaction provides one of the few examples of asymmetric induction caused by molecular asymmetry. For other examples, see J. A. Berson and M. A. Greenbaum, *ibid.*, 80, 445, 653 (1958), and 81, 6456 (1959).

(6) E. M. Kosower and S. Winstein, *ibid.*, 78, 4347 (1956).

(7) D. J. Cram, R. H. Bauer, N. L. Allinger, R. A. Reeves, W. J. Wechter, and E. Heilbronner, *ibid.*, 81, 5977 (1959).

Table I. First-Order Rate Constants and Activation Parameters for Solvolyses
of Trichloroacetates of III-α and III-β and Tosylates of IV-α and IV-β

Run no.	Ester of	Solvent	Temp, °C	$k \times 10^6$, sec^{-1} a	$\Delta H^{\ddagger}$, kcal/mole	$\Delta S^{\ddagger}$, eu
1	III-α	O(CH$_2$CH$_2$)$_2$O–H$_2$O^c	24.82	5.27 ± 0.07		
2	III-α	O(CH$_2$CH$_2$)$_2$O–H$_2$O^c	49.69	79.0 ± 1.0	20.2 ± 0.2^b	−14.9 ± 0.7^b
3	III-β	O(CH$_2$CH$_2$)$_2$O–H$_2$O^c	24.82	5.84 ± 0.06		
4	III-β	O(CH$_2$CH$_2$)$_2$O–H$_2$O^c	50.04	94.4 ± 2.1	20.5 ± 0.2^b	−13.6 ± 0.8^b
5	IV-α	CH$_3$CO$_2$H	49.99	9.68 ± 0.04		
6	IV-α	CH$_3$CO$_2$H	74.97	172 ± 1	25.1 ± 0.4^d	−4.1 ± 1.2^d
7	IV-β	CH$_3$CO$_2$H	49.99	8.97 ± 0.05		
8	IV-β	CH$_3$CO$_2$H	74.97	156 ± 1	24.9 ± 0.6^d	−4.9 ± 1.6^d

^{a} Average of two runs. Standard deviations were used for ± values (see Experimental Section). ^{b} Calculated at 24.82° (see Experimental Section). ^{c} Solvent 9:1 dioxane–water by volume. ^{d} Calculated at 74.97°.

Table II. Solvolysis Products of Trichloroacetates and Methyl Ethers of
III-α and III-β and of Tosylate Esters of IV-α and IV-β

Run no.	Compd solvolyzed	Solvent	Temp, °C	Time, hr	% yield sol prodt	% yield olefin	—Prodt compstn— % α	% β
9	III-α-TCA^a	O(CH$_2$CH$_2$)$_2$O–H$_2$O^b	50	100	81	12	50	50
10	III-β-TCA^a	O(CH$_2$CH$_2$)$_2$O–H$_2$O^b	50	100	75	7	50	50
11	III-α-TCA^a	CH$_3$OH	65	11	89	1.4	56	44
12	III-β-TCA^a	CH$_3$OH	65	11	81	1.4	57	43
13	III-α-TCA^a	CH$_3$OH–KOAc^c	65	1.75	97	1.3	24	76
14	III-β-TCA^a	CH$_3$OH–KOAc^c	65	1.75	92	0.4	30	70
15	III-α-CH$_3$^{d}	CH$_3$OH–Cl$_3$CCO$_2$H^e	65	10	90	...	60	40
16	III-β-CH$_3$^{d}	CH$_3$OH–Cl$_3$CO$_2$H^e	65	10	95	...	53	47
17	IV-α-Ts^f	AcOH	75	18	92	3.4	97.4	2.6
18	IV-β-Ts^f	AcOH	75	18	91	4.7	7.2	92.8
19	IV-α-Ts^f	HCO$_2$H–NaO$_2$CH^g	75	7	76	...	>99	<1
20	IV-β-Ts^f	HCO$_2$H–NaO$_2$CH^g	75	7	78	...	<1	>99

^{a} Trichloroacetate of alcohols III-α or III-β. ^{b} 9:1 dioxane–water by volume. ^{c} 1.4 moles based on substrate = 1 mole. ^{d} Methyl ethers of III-α and III-β. ^{e} 0.0115 M. ^{f} Tosylates of IV-α and IV-β. ^{g} 0.025 M.

mp 88.7–89.3° (acetate is eluted less rapidly from silica gel). The relative configurations of these alcohols are provisionally assigned in the Discussion. The tosylates of IV-α and IV-β were easily prepared and handled.
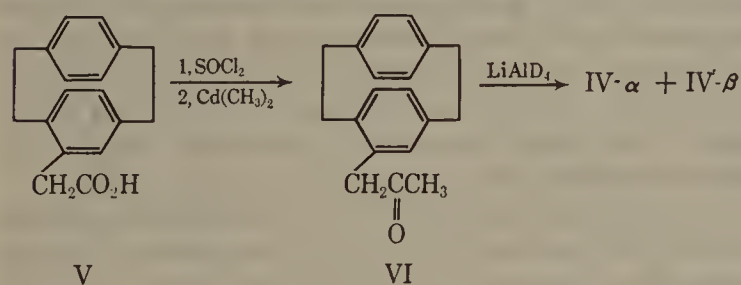
Kinetics. Table I summarizes the kinetic results of hydrolysis in 9:1 dioxane–water (by volume) of the trichloroacetates of III-α and III-β. The reactions exhibited good first-order kinetics (nine points per run) as followed by titration of the liberated trichloroacetic acid with standard base.[6] Activation parameters were calculated from rate constants determined at 25 and 50°.

The kinetics of acetolysis of tosylates of IV-α and IV-β were studied at 50 and 75°. Good first-order rate constants (minimum of ten points) were obtained by titrating the liberated p-toluenesulfonic acid with standard sodium acetate in glacial acetic acid. The rate constants and the derived activation parameters are listed in Table I.

Products of Solvolyses. The trichloroacetates of III-α and III-β were hydrolyzed in 9:1 dioxane–water for 100 hr at 50° to produce a mixture of epimeric

alcohols (III-α and III-β) and a minor amount of olefin. Control runs demonstrated that these compounds once formed did not epimerize. Table II reports the yields and the relative amounts of the epimeric alcohols produced. The analysis of the alcoholic mixtures made use of the difference in the nmr spectra of α- and β-III.

Each of the epimeric trichloroacetates was also subjected to methanolysis, both with and without added potassium acetate to neutralize the trichloroacetic acid developed. The methyl ethers produced were analyzed by nmr methods, and Table II records the results. The product distribution varied significantly when potassium acetate was added. Control runs indicated that the methyl ethers epimerize under the conditions of the methanolysis in the absence of potassium acetate to neutralize the acid produced. Indeed, in runs 11 and 12, epimeric equilibrium of the methyl ethers was reached in the course of methanolyses run in the absence of potassium acetate, and the α isomer proved to be the more stable of the two (see also runs 15 and 16). Attempts to epimerize to equilibrium alcohols III-α and III-β with aluminum isopropoxide and acetone in 2-propanol[8] were unsuccessful; III-α epimerized only about 10–15%, while III-β gave a mixture of about 52% α, 48% β.

The tosylate esters of IV-α and IV-β were subjected to acetolysis at 75° for 18 hr and the acetate products analyzed (see Table II). Control experiments demon-

(8) (a) W. G. Dauben, G. J. Fonken, and D. S. Noyce, *J. Am. Chem. Soc.*, 78, 2579 (1956); (b) E. L. Eliel and R. S. Ro, *ibid.*, 79, 5992 (1957).

strated that the product acetates did not epimerize under the conditions of the acetolysis. The two tosylate esters also were subjected to formolysis at 75° for 7 hr in the presence of 1.05 equiv of sodium formate. The product formates were then reduced to the alcohols with lithium aluminum hydride and converted to their acetates for analysis. The product distributions are listed in Table II.

Discussion

The solvolysis of the tosylate esters of IV-α and IV-β will be discussed first, and an argument presented for the relative configurations for the two epimers. It will be demonstrated that most of the reaction with acetic acid and essentially all of the reaction in formic acid occur *via* the phenonium ion. The solvolysis of the trichloroacetate esters of III-α and III-β will then be discussed, and a provisional assignment of relative configurations of the epimers made.

[2.2]Paracyclophanyl Nucleus as a Neighboring Group. In the acetolysis of the tosylate esters of IV-α and IV-β *retention dominated over inversion of configuration by factors of 37.4 and 12.9, respectively* (runs 17 and 18, Table II). In ordinary simple acetolysis of tosylate esters of secondary alcohols which contain no neighboring groups, *inversion predominates over retention of configuration* by substantial factors.[9] Even more striking are the formolyses results. In formic acid the epimeric tosylates gave formates with retention of configuration by factors of greater than 100. Nothing in open carbonium ion theory provides an explanation for these results, either for the high retention observed, or for the higher stereospecificity observed in formic (less nucleophilic solvent) than in acetic acid. These stereochemical results alone require the intervention of a phenonium ion as a discrete intermediate[10] in these solvolysis reactions.

The interesting question arises as to whether the π electrons between the two benzene rings or on the external faces of the paracyclophane nucleus aid in displacement of the tosylate group. Each of the two possibilities leads to a different type of phenonium ion, the former to A and the latter to B. Of these, B seems the more probable for two reasons. (1) The bending of the benzene rings into a tub[11] represents a slight rehybridization of the π electrons in the direction of sp³, and thus the external faces of the benzene rings should be more nucleophilic than the internal. (2) Phenonium ion B is much less sterically compressed than phenonium ion A.

Intermediates in which the transannular benzene ring also becomes directly involved in bridged ion formation can also be envisioned, but are considered unlikely for reasons enumerated in earlier studies.[2]

Implicit in the structures of B-α and B-β are the relative configurational assignments of the starting materials and products since each diastereomeric phenonium ion is formed and decomposed with inversion at secondary carbon. Since two inversions are the equivalent of one retention, the stereochemical results and the bridged ion theory are compatible. The small amount of simple inversion observed in the acetolysis

(9) A. Streitwieser, Jr., "Solvolytic Displacement Reactions," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, pp 59, 73.
(10) D. J. Cram, *J. Am. Chem. Soc.*, 71, 3863 (1949).
(11) C. L. Coulter and K. N. Trueblood, *Acta Cryst.*, 16, 667 (1963).
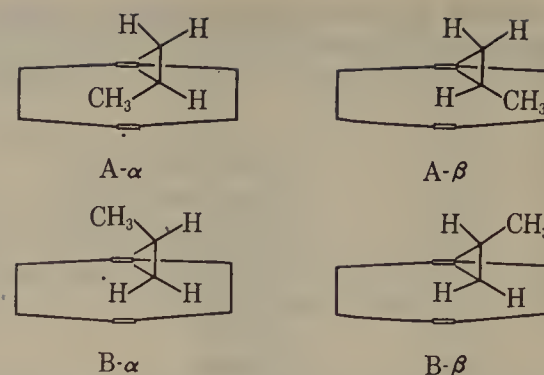
provides a measure of how much open ion was produced compared to the bridged ion.

The relative configurations assigned to B-α and B-β and hence to IV-α and IV-β (and their respective tosylates) are based on two considerations. (1) The tosylate of IV-α solvolyzes ~10% faster than that of IV-β (see Table I, runs 6 and 8). Molecular models suggest that whereas the diastereomeric starting states should be close to one another in energy, B-α and B-β should be somewhat different, with the α bridge being the more stable. Thus, the steric interference between the methyl and methylene groups in B-β is more severe than those in B-α. (2) Compatible with this interpretation is the fact that the faster acetolyzing isomer (α configuration) also gives the higher stereospecificity by a factor of about 3 (37.4:12.9). Thus, the higher energy bridged ion (B-β configuration) should compete with open ion formation less successfully than the more stable bridged ion (B-α configuration).

The tosylate of IV-α acetolyzes at 75° 13 times faster than 1-phenyl-2-propyl tosylate,[12] while that of IV-β goes about 12 times faster. In spite of the greater steric compression in forming bridged ions from the paracyclophanyl system than the simple phenyl system, bridged ions have a greater tendency to form from the former system. This conclusion derives from the above rate comparisons as well as from stereochemical comparisons. Thus, acetolysis of 1-phenyl-2-propyl tosylate proceeded with 65% inversion and 35% retention,[12] or retention:inversion = 0.54, as compared to factors of 37.4 and 12.9 for the tosylates of IV-α and IV-β. Again, conformity between conclusions based on kinetic and stereochemical comparisons are evident.

The enhanced ability of the [2.2]paracyclophanyl nucleus to act as a neighboring group probably derives from several factors. Charge delocalization into the transannular ring in the transition state for bridge ion formation and release of some puckering strain are two factors that probably operate. Other work has demonstrated the [2.2]paracyclophane nucleus to be a better π base toward both tetracyanoethylene[13] and strong electrophiles than open-chain model compounds.

Effect of [2.2]Paracyclophane Nucleus on Stereochemistry of Solvolysis at Attached Carbon. An examination of scale molecular models of the epimeric alcohols III indicates that the preferred conformation of the hydroxyl-substituted carbon has the methine hydrogen atom between the two aromatic rings (in the projection formula) and the hydroxyl and methyl groups above the plane of the substituted ring. Furthermore, because the

(12) S. Winstein, M. Brown, K. C. Schreiber, and A. H. Schlesinger, *J. Am. Chem. Soc.*, 74, 1140 (1952).
(13) (a) D. J. Cram and R. H. Bauer, *ibid.*, 81, 5971 (1959); (b) D. J. Cram, W. J. Wechter, and R. W. Kierstead, *ibid.*, 80, 3126 (1958).

o-methylene is larger than the *o*-hydrogen, the groups above the ring (in profile) are probably rotated somewhat away from the nearest methylene bridge. The configurations indicated in formulas C and D are assigned to the experimentally designated III-α and III-β diastereomeric racemates on the basis of equilibrium data and chromatographic behavior.

C or III-α   D or III-β
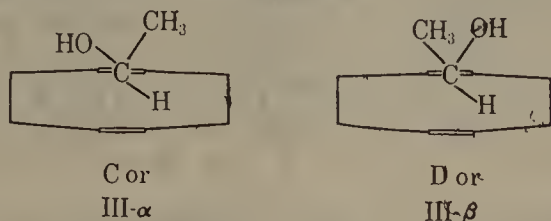
The methyl ethers of III-α and III-β when treated with trichloroacetic acid in methanol each gave a mixture of epimers in which the α isomer predominated (see runs 15 and 16, Table II). In the methanolysis of the epimeric trichloroacetates in the absence of potassium acetate (runs 11 and 12), the same mixture of ethers was obtained, 57% α and 43% β. Furthermore, III-β when treated with acetone–aluminum isopropoxide gave an epimeric mixture in which III-α dominated. Thus, the α isomers appear to be the more thermodynamically stable by a small amount. Since molecular models suggest that configuration C is more stable than D, the tentative configurational assignment is possible.

The III-α isomer was experimentally designated as being the one that moved faster on a chromatograph column. Examination of scale models of the conformation formulated indicates that the hydroxyl group of C is more exposed to absorbing centers than that of D, and thus the faster moving isomer, III-α, probably possesses the configuration of formula C, and III-β that of D.

These assignments allow the other properties of III-α and III-β to be given a structural interpretation. Thus, the methyl group of III-α absorbs in the nmr at τ 8.76 and the hydroxyl group at τ 8.12, whereas the methyl of III-β absorbs at τ 8.46 and the hydroxyl at τ 8.42. The model compound, 1,4-dimethyl-2-(α-hydroxyethyl)benzene, exhibits a carbinyl methyl signal at τ 8.68 which is between the two diastereomers. In formula C, the methyl group is expected to be more shielded by the ring current than the methyl group in D, and conversely for the hydroxyl group. Thus, assignment of structures C and D to compound III-α and III-β is compatible with the nmr spectra. Similar arguments apply to the methyl ethers and trichloroacetates of the epimeric alcohols.

The nmr spectra of III-α and III-β and their respective ethers and trichloroacetates provide further structural correlations. All α epimers produce a downfield shift of the *ortho* proton, the shift being most noticeable in the trichloroacetate. All β epimers exhibit a downfield shift of a fraction of one proton of the methylene bridges as a multiplet consisting of several small peaks. These two effects suggest an interaction of the protons with the oxygen function, which in each case is a near neighbor of the proton in question. Such effects have been noted in similar systems, and will be reported in a later paper in this series.[14]

The trichloroacetate of III-β underwent hydrolysis at a rate about 12% faster than that of the III-α isomer

at 50° (runs 2 and 4 of Table I). Although this rate difference is disappointingly small, it is compatible with the configurational assignments if the trichloroacetate group leaves in a transition state with that group *trans* to the transannular benzene ring. Such a transition state provides for coplanarity of the carbonium ion substituents and the attached benzene ring. The ion from the α configuration should be more compressed than that from the β configuration.

The product data for the hydrolyses of the trichloroacetates of III-α and III-β indicate that III-α and III-β are produced in exactly equal amounts from either diastereomeric ester (runs 9 and 10 of Table II). The fact that both diastereomers produce exactly the same balance of products suggests that the two diastereomeric, coplanar carbonium ions equilibrate. The fact that this balance of products was 1:1 indicates that over-all water capture by the carbonium ion occurred without any asymmetric induction.

In the methanolysis reactions carried out under conditions of kinetic control of products, the ester of III-α gave a product balance in which the ether of III-β predominated over that of III-α by a factor of 3.1. This factor decreased to 2.3 when the ester of III-β was starting material (runs 14 and 15 of Table II). The two carbonium ions appear to have nearly equilibrated in methanol, and some asymmetric induction is apparent in the methanol capture process. The predominance of the β ether in the product is compatible with the predominant capture of the sterically least compressed coplanar carbonium ion from the least hindered side (the side remote from the transannular benzene ring).

Both of the above sets of results are significantly different from those obtained from α-phenylethyl systems, in which inversion is the net steric course under a variety of conditions.[15] For example, α-phenylethyl tosylate undergoes ethanolysis with 20% net inversion. The absence of high degrees of stereospecificity and rate differences in the solvolyses reactions contrast with the results of Richards and Hill,[16] who observed both in solvolyses of the α-acetoxy-1,1'-trimethyleneferrocene diastereomers.

The small predominance of III-α over III-β (factor of 1.3) in the product of lithium aluminum hydride reduction of 4-acetyl[2.2]paracyclophane is compatible with the notion that in the predominant product-determining transition state, the oxygen of the carbonyl group complexed to metal is oriented toward the least hindered position in the molecule, and the hydrogen then approaches the carbonyl group from the side of least hindrance.[17]

Experimental Section

The syntheses described here were usually repeated and the best conditions recorded. Melting points and boiling points are uncorrected. Silica gel G layers, 0.25 mm thick on glass plates, were used in thin layer chromatography (tlc). The plates were developed in an iodine chamber. All infrared spectra were recorded on a Beckman IR-5 spectrophotometer. Solutions were 5–10% in spectrograde chloroform as solvent. Crude [2.2]paracyclophane[18] was

(14) H. Reich, unpublished work.

(15) For a summary, see ref 9.
(16) J. H. Richards and E. A. Hill, *J. Am. Chem. Soc.*, 81, 3484 (1959); 83, 3840, 4216 (1961).
(17) D. J. Cram and K. R. Kopecky, *ibid.*, 81, 2748 (1958), and references cited therein.
(18) D. J. Cram and H. Steinberg, *ibid.*, 73, 5691 (1951).

crystallized by Soxhlet extraction with chloroform to give octahedra, mp 286–287°. Reagent grade chloroform, dichloromethane, acetone, and methanol were used directly. Diethyl ether was anhydrous Mallinckrodt Analytical Reagent. Pyridine was Karl Fischer reagent grade (Matheson Coleman and Bell), stored over potassium hydroxide pellets. Technical pentane was distilled before use. Dioxane was purified by the method of Fieser[19] and distilled from sodium just prior to use.

Mallinckrodt Analytical Reagent trichloroacetic acid was crystallized from benzene and stored over anhydrous magnesium perchlorate in a vacuum desiccator to give material, mp 59–59.5° (lit.[20] mp 59.5–60.3°). Benzene was distilled from sodium and stored over sodium. Dry acetic acid for acetolysis reactions was prepared by refluxing glacial acetic acid with 3% by weight acetic anhydride for 12 hr and distilling; a center cut was taken, bp 117.1°, and this material was made 1% by weight in freshly distilled acetic anhydride. Formic acid (Baker, 98%) was allowed to stand over boric anhydride for 48 hr, filtered, and distilled from molecular sieves, and a center cut was retained, bp 100.2°.

4-Acetyl[2.2]paracyclophane. A modification of the reported method[4] was employed. A solution of 107.2 g of aluminum chloride (0.96 mole) and 74.8 g of acetyl chloride (0.80 mole) in 800 ml of dichloromethane was cooled to −15°, and 100 g (0.48 mole) of [2.2]paracyclophane was added in one quick addition with efficient mechanical stirring. The temperature was maintained at −20 to −15° for 6 min, and the blood-red reaction mixture was poured into ice–dilute hydrochloric acid. The aqueous layer was separated and extracted with fresh dichloromethane. The organic layers were combined, washed successively with dilute hydrochloric acid, water, saturated aqueous sodium bicarbonate, water, and twice with saturated aqueous sodium chloride, and dried. Solvent was evaporated to leave a yellowish solid which was crystallized from ether to yield 61.0 g (51%) of hard white crystals of the desired ketone, mp 108.5–109.5° (lit.[4] 109.7–110.4°). The mother liquors were concentrated to a viscous yellow oil which was chromatographed over 1.2 kg of silica gel. Elution with 2.5 l. of ether–pentane (25:75) produced a trace of starting material; the next 6.4 l. eluted 22.5 g (18.5%) of additional ketone, mp 108–109°.

4-(1-Hydroxyethyl)-[2.2]paracyclophane (III) and Separation of Diastereoisomers. A 126.6-g portion (0.507 mole) of the above crude ketone, mp 104–108°, was dissolved in a solution of ether and 330 ml of tetrahydrofuran and added dropwise over 2 hr at 25° to a stirred mixture of 20 g (0.53 mole) of lithium aluminum hydride in 150 ml of ether. After addition, the mixture was stirred at 25° for 30 hr and then was carefully hydrolyzed by the addition of saturated aqueous potassium carbonate. The ether layer was washed once with 2% hydrochloric acid and twice with saturated aqueous sodium chloride and dried. Solvent was evaporated to leave 125.9 g of an oil which, except for 2.9 g of residual [2.2]paracyclophane, was dissolved in boiling ether and allowed to stand in the cold until 55 g of white solid (mp 55–110°) separated. The noncrystalline portion (68 g) of the above product was chromatographed on 2540 g of activity 2 alumina. Elution with solvent ranging from ether–pentane 10:90 to ether–pentane 30:70 produced 16.4 g of side products. Elution with solvent ranging from ether–pentane 40:60 to pure ether produced 30.4 g of pure diastereomer α of 4-(1-hydroxyethyl)-[2.2]paracyclophane, III-α, transparent plates, mp 107–107.5° (vide infra). Finally, elution with pure ether and then methanol–dichloromethane (5:95) produced 13.0 g of alcohol III enriched in diastereomer β; several crystallizations of this material from ether yielded 4.4 g of pure III-β, mp 117–118° (vide infra).

The 55-g portion of white solid mentioned above was chromatographed over 1800 g of Woelm neutral activity 1 alumina. Elution with solvent ranging from ether–pentane 20:80 to pure ether produced 4.0 g of side products. Further elution with ether and then with dichloromethane–ether (3:97) produced 2.5 g of III-α. Elution with dichloromethane–ether (10:90), methanol–dichloromethane (5:95), and finally methanol produced 40.6 g of alcohol III enriched in diastereomer III-β. Several crystallizations of this material from hexane–chloroform yielded 11.8 g of alcohol III-β as fine white needles, mp 117–118°.

Alcohol diastereomer III-α exhibited the usual hydroxyl absorption at 2.8 and 2.9 μ in the infrared. The nmr spectrum was as follows: seven protons as a multiplet at τ 3.25–3.83 (aromatic),

one proton as a quartet (J = 6.5 cps) at τ 5.11 (methine), eight protons as a multiplet at τ 6.50–7.44 (bridge), one proton as a singlet at τ 8.12 (hydroxyl), and three protons as a doublet (J = 6.5 cps) at τ 8.76 (methyl). This material had R_f 0.5 on tlc with solvent system pentane–ether–methanol (65:30:5). Anal. Calcd for $C_{18}H_{20}O$: C, 85.67; H, 7.99. Found: C, 85.47; H, 8.21.

Alcohol diastereomer III-β exhibited the usual hydroxyl absorption at 2.8 and 2.9 μ in the infrared. The nmr spectrum was as follows: seven protons as a multiplet at τ 3.37–3.91 (aromatic), one proton as a quartet (J = 6.5 cps) at τ 5.23 (methine), eight protons as a multiplet at τ 6.20–7.50 (bridge), one proton as a singlet at τ 8.42 (hydroxyl) overlapped by three protons as a doublet (J = 6.5 cps) at τ 8.46 (methyl). This material had R_f 0.4 on tlc with solvent system pentane–ether–methanol (65:30:5). Anal. Calcd for $C_{18}H_{20}O$: C, 85.67; H, 7.99. Found: C, 85.67; H, 8.20.

A solution of 3.00 g of 4-acetyl[2.2]paracyclophane, mp 108.5–109.5°, in 100 ml of ether was added dropwise to a stirred mixture of 0.75 g of lithium aluminum hydride in 250 ml of ether. The reaction mixture was stirred for 2 hr and carefully hydrolyzed by the addition of 100 ml of saturated aqueous magnesium sulfate. The aqueous layer was separated and extracted with another portion of ether, and the ether layers were combined, washed with water, and dried. Evaporation of solvent left 3.08 g of alcohol III as a clear oil which slowly became a white solid, mp 64–76°. A sample of the oil was analyzed by nmr and shown to be 57% alcohol III-α and 43% III-β.

When the same reaction was repeated with "inverse addition" (760 mg of lithium aluminum hydride in ether slurry added to 500 mg of ketone in ether), followed by similar isolation, the product alcohol (white solid, mp 55–75°) was shown by nmr analysis to be 67% alcohol III-α and 33% III-β.

Attempted Thermodynamic Equilibration of Diastereoisomers of 4-(1-Hydroxyethyl)-[2.2]paracyclophane (III). To 50 ml of dry isopropyl alcohol (distilled from calcium oxide) were added 1.00 g (4 mmoles) of alcohol III-β, 0.81 g (4 mmoles) of freshly distilled aluminum isopropoxide, and 1 ml of acetone. The mixture was refluxed for 122 hr, and an aliquot was withdrawn and analyzed by tlc [pentane–ether–methanol (65:30:5) solvent system]. Approach to an equilibrium alcohol mixture seemed to be very slow, even after refluxing for an additional month, so the contents of the reaction flask were sealed in a tube which was then heated at 123° for 6.5 days. The tube was cooled and opened, and the contents were poured into 250 ml of water containing 10 ml of concentrated hydrochloric acid. This mixture was extracted with two 100-ml portions of ether. The ether extracts were combined, washed with water and 5% aqueous sodium bicarbonate, and dried. Solvent was removed to leave a yellow oil which tlc showed to contain alcohols III-α and III-β plus two unidentified components. The mixture was chromatographed over a short column of activated silica gel. Elution with ether–pentane 2:98 produced two unidentified components; elution with ether-pentane 30:70 afforded 500 mg of white solid. Analysis of this material showed it to be approximately 52% alcohol III-α and 48% III-β.

Trichloroacetates of 4-(1-Hydroxyethyl)-[2.2]paracyclophane. To 10 ml of dry pyridine was added 1.50 g (5.96 mmoles) of alcohol III-α, and the solution was cooled to 0°. To 5 ml of dry pyridine, which had been cooled to 0°, was added 1.2 ml of trichloroacetyl chloride (Eastman White Label, ca. 11 mmoles) to produce a yellow solution. The trichloroacetyl chloride solution was poured into the alcohol solution, and the reaction mixture was kept at 0° for 15 min with occasional swirling; a precipitate of pyridine hydrochloride formed almost immediately. The reaction mixture was poured into 75 ml of ice water containing 0.75 g of potassium bicarbonate. The yellow solid which separated was extracted with three 125-ml portions of 3:1 ether–pentane, and the combined organic extracts were washed with ice-cold 5% hydrochloric acid (three 75-ml portions), ice-cold 5% aqueous sodium bicarbonate (two 75-ml portions), ice-cold water, and ice-cold saturated aqueous sodium chloride, and dried. Solvent was removed at reduced pressure to leave 2.33 g (99%) of crude yellow, waxy solid which was dissolved in about 15 ml of pentane containing some ether. After 2 days at −20° were deposited hard, transparent prisms. These were collected and recrystallized to give prisms of trichloroacetate of III-α, mp 82–82.5° dec. This compound decomposed at room temperature within a few days but could be stored indefinitely at −20°.

The infrared spectrum of this trichloroacetate showed bands at 5.70 (strong), 7.97 (strong), and 8.2 μ (shoulder). The nmr spectrum was as follows: one proton as a broad singlet at τ 3.33 (ortho

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(19) L. F. Fieser, "Experiments in Organic Chemistry," D. C. Heath and Co., Boston, Mass., 1957, p 284.

(20) E. Grunwald and E. Price, J. Am. Chem. Soc., **86**, 4517 (1964).

proton) and six protons as a multiplet at τ 3.40-3.64 (aromatic), one proton as a quartet (J = 6.5 cps) at τ 3.84 (methine), eight protons as a multiplet at τ 6.56-7.34 (bridge), and three protons as a doublet (J = 6.5 cps) at τ 8.62 (methyl). *Anal.* Calcd for $C_{20}H_{19}Cl_3O_2$: C, 60.40; H, 4.81; Cl, 26.74. Found: C, 60.58; H, 4.73; Cl, 26.98.

Exactly as in the procedure described above, 1.50 g of alcohol III-β was converted to its trichloroacetate. This material was isolated as a yellow solid in crude yield of 2.30 g (98%); two crystallizations from ether–chloroform at −20° yielded a voluminous white solid, mp 92.4-92.8° dec (heating rate *ca.* 2°/min; the melting point was dependent on heating rate). This compound decomposed at room temperature within a few days but could be stored indefinitely at −20°.

The infrared spectrum of the trichloroacetate of III-β showed bands at 5.69 (strong), 8.03 (strong), and 8.2 μ (shoulder). The nmr spectrum was as follows: seven protons as a multiplet at τ 3.33-3.77 (aromatic) slightly overlapping one proton as a quartet (J = 6.5 cps) at τ 3.94 (methine), eight protons as a multiplet at τ 6.44-7.30 (bridge), and three protons as a doublet (J = 6.5 cps) at τ 8.28. *Anal.* Calcd for $C_{20}H_{19}Cl_3O_2$: C, 60.40; H, 4.81; Cl, 26.74. Found: C, 60.52; H, 4.74; Cl, 27.01.

β-4-(1-Methoxyethyl)-[2.2]paracyclophane. To a flask were added 0.500 g (2.0 mmoles) of alcohol III-β, 1.22 g (8.0 mmoles) of barium oxide, 1.25 ml (20 mmoles) of methyl iodide, 10 ml of dimethylformamide, and 0.05 ml of water. This mixture was stirred for 27 hr at 25°; after 6.5 hr of this period, an additional 1.25 ml of methyl iodide was added. The yellow reaction mixture was poured into 75 ml of chloroform, washed twice with water, once with dilute aqueous sodium bisulfite, again with water, and once with saturated aqueous sodium chloride, and dried. Solvent was evaporated, and the residue was chromatographed over 40 g of activated silica gel. Elution with ether–pentane 1:99 produced *ca.* 1 mg of a substance which appeared to be α-4-(1-methoxyethyl)-[2.2]paracyclophane; ether–pentane 3:97 eluted 252 mg (48%) of β ether; ether–pentane 50:50 eluted 191 mg of unreacted alcohol III-β.

The ether of III-β was crystallized from ether–pentane to yield a white solid, mp 64.8-65.5°. The infrared spectrum exhibited a band at 9.1 μ (medium, antisymmetric C–O–C stretching).[21] The nmr spectrum was as follows: seven protons as a multiplet at τ 3.40-3.84 (aromatic), one proton as a quartet (J = 6.5 cps) at τ 5.61 (methine), three protons as a sharp singlet at τ 6.92 (methoxy) superimposed on eight protons as a multiplet at τ 6.36-7.43 (bridge), and three protons as a doublet (J = 6.5 cps) at τ 8.47 (methyl). *Anal.* Calcd for $C_{19}H_{22}O$: C, 85.67; H, 8.33. Found: C, 85.61; H, 8.18.

Methanolysis of Trichloroacetates of 4-(1-Hydroxyethyl)-[2.2]-paracyclophane. A. Without Added Potassium Acetate. A solution of 750 mg of trichloroacetate of III-α in 195 ml of methanol was refluxed for 11 hr, cooled, and shaken with a mixture of 100 ml of chloroform and 200 ml of water. The aqueous layer was separated and extracted with another portion of chloroform. The chloroform extracts were combined, washed with water, and dried. Evaporation of solvent left a yellow oil which was chromatographed over a short column of activated alumina. Elution with pentane produced 6 mg of material which was apparently olefinic (infrared analysis) but which was not further characterized; then ether–pentane (7.5:92.5) eluted 447 mg (89%) of a colorless oil which was shown by tlc [ether–pentane (10:90) solvent system] to be two components. Nmr analysis showed this mixture to be 56% ether of III-α (*vide infra*) and 44% ether of III-β

A similar run was made with 500 mg of trichloroacetate of III-β in 130 ml of methanol. Similar work-up and chromatography produced 4 mg of the apparent olefin and 270 mg (81%) of a slightly yellow oil which nmr analysis showed to be 57% ether of III-α (*vide infra*) and 43% ether of III-β.

The above two product oils were combined and a *ca.* 650-mg portion of the mixture was chromatographed over 40 g of activated silica gel. Elution with ether–pentane 1:99 provided 338 mg of ether of III-α and elution with ether–pentane 7.5:92.5 provided 298 mg of ether of III-β, mp 64.5-65.5°.

The ether of III-α was a white solid which was crystallized from pentane–ether, mp 63.5-64.1°. The infrared spectrum showed bands at 8.9 and 9.15 μ (medium, antisymmetric C–O–C stretching).[21] The nmr spectrum was as follows: seven protons as a multiplet at τ 3.33-3.72 (aromatic), one proton as a quartet (J

= 6.5 cps) at τ 5.73 (methine), three protons as a sharp singlet at τ 6.45 (methoxy), eight protons as a multiplet at τ 6.51-7.40 (bridge), and three protons as a doublet (J = 6.5 cps) at τ 8.79 (methyl). *Anal.* Calcd for $C_{19}H_{22}O$: C, 85.67; H, 8.33. Found: C, 85.49; H, 8.17.

B. With Added Potassium Acetate. To 125 ml of methanol were added 507 mg (1.28 mmoles) of trichloroacetate of III-α and 177 mg (1.80 mmoles) of freshly fused potassium acetate. The mixture was refluxed for 105 min, cooled, and worked up as described in part A above. Chromatography of the yellow oil, as described above, provided 4 mg of the presumed olefin and 300 mg (97%) of a colorless oil which was a mixture of the diastereomeric ethers by tlc. Nmr analysis showed this mixture to be 24% α ether and 76% β ether.

Similarly, 409 mg (1.03 mmoles) of trichloroacetate of III-β and 142 mg (1.45 mmoles) of freshly fused potassium acetate were refluxed in 100 ml of methanol for 105 min and worked up as above. Chromatography as described provided 1 mg of the presumed olefin and 252 mg (92%) of a slightly yellow oil which was a mixture of the diastereomeric ethers by tlc. Nmr analysis of this mixture showed it to be 30% α ether and 70% β ether. ·

Trichloroacetic Acid Catalyzed Epimerization of α- and β-4-(1-Methoxyethyl)-[2.2]paracyclophane. To 20 ml of methanol were added 61 mg (0.23 mmole) of α ether and 38 mg (0.23 mmole) of trichloroacetic acid. The solution was refluxed for 10 hr, cooled, and shaken with a mixture of 75 ml of 1:1 ether–pentane and 75 ml of water. The aqueous layer was separated and extracted with another portion of the ether–pentane. The organic layers were combined, washed with water, and dried. Removal of solvent left a yellow oil which was chromatographed on a short column of activated silica gel. Elution with ether–pentane (5:95) produced 55 mg of an oil which tlc showed to be a mixture of the diastereomeric ethers. Nmr analysis of this mixture showed it to be 60% α ether and 40% β ether.

A similar reaction with 125 mg (0.47 mmole) of β ether, 77 mg (0.47 mmole) of trichloroacetic acid, and 40 ml of methanol provided 118 mg of a yellow oil which, after chromatography, proved by nmr analysis to be 53% α ether and 47% β ether.

Kinetics of Hydrolysis of Trichloroacetates of 4-(1-Hydroxyethyl)-[2.2]paracyclophane. Solutions of trichloroacetates of III-α and of III-β were prepared in concentrations of 0.01006 M (0.01474 M for the β isomer at 50°) by weighing the appropriate amounts of material into volumetric flasks and diluting to the mark with 9:1 dioxane–water (by volume). Aliquots were then withdrawn with an automatic pipet and sealed into clean ampoules. The ampoules were placed in thermostated baths at the indicated temperatures and removed at the designated times (from immersion to removal), swirled in ice water, and then stored at −20° until all tubes in a run could be titrated in sequence. The tubes were opened, diluted with 15 ml of water, and titrated to the phenolphthalein end point with 0.02564 N sodium hydroxide. End points tended to drift and infinity titrations were always low so that theoretical infinity values were used.

The data were analyzed by a least-squares program on the IBM 7094 computer, and standard deviations are listed with the calculated first-order rate constants. The rate constants for two runs were averaged, along with their standard deviations, and thermodynamic functions (see Table I) were calculated in the usual way. Limits on these functions were determined, using the rate-constant standard deviations, by the method of total differentials.[22] Table III contains a representative sample of the data obtained.

Hydrolysis of Trichloroacetates of 4-(1-Hydroxyethyl)-[2.2]-paracyclophane. A 1.00-g sample of trichloroacetate of III-α was dissolved in 250 ml of 9:1 dioxane–water (by volume) and placed in a constant temperature bath at 50° for 100 hr. The reaction mixture was then poured into 500 ml of water and extracted with four 150-ml portions of 3:1 ether–pentane. The combined extracts were washed three times with saturated aqueous sodium chloride and dried. Solvent was evaporated at reduced pressure to leave a yellow oil which was chromatographed over a short column of activated silica gel. Elution with pentane provided 70 mg (12%) of 4-vinyl[2.2]paracyclophane (*vide infra*), and ether–pentane (30:70) eluted 514 mg (81%) of a white solid, mp 72-89°, which infrared analysis and tlc [pentane–ether–methanol (65:30:5) solvent system, iodine detector] showed to be a mixture of alcohols III-α and III-β. Control experiments showed these alcohols to

(21) K. Nakanishi, "Infrared Absorption Spectroscopy," Holden-Day, Inc., San Francisco, Calif., 1962, p 36.

(22) L. L. Smail, "Analytical Geometry and Calculations," Appleton-Century-Crofts, New York, N. Y., 1953, p 544.

Table III. Kinetics of Hydrolysis of Trichloroacetate of III-α at 24.82 ± 0.01°, Concentration 0.01006 M, Aliquot Size 4.90 ml, Theoretical Infinity 1.922 ml

Run a NaOH, ml	Time, min	Run b NaOH, ml
0.251	129.68	0.221
0.352	406.0	0.345
0.463	717.0	0.468
0.734	1376.0	0.746
0.980	2165.0	0.960
1.223	3029.0	1.248
1.426	4080.0	1.400
1.553	5088.0	1.572
1.782	7939.0	1.770
$k = 5.31 \pm 0.06$ $\times 10^{-6}$ sec^{-1}		$k = 5.22 \pm 0.08$ $\times 10^{-6}$ sec^{-1}
	Av $k = 5.27 \pm 0.07 \times 10^{-6}$ sec^{-1}	

be stable to silica gel chromatography. Nmr analysis of this mixture showed it to be 50% III-α and 50% III-β.

A duplicate run also provided 12% of olefin V and 81% of a mixture of alcohols III-α and III-β (mp 72–89°), which nmr analysis showed to be 49% III-α and 51% III-β.

A 1.00-g sample of trichloroacetate of III-β in 250 ml of 9:1 dioxane–water was treated in a manner identical with that described above. The yellow residue was chromatographed over a short column of activated silica gel. Elution with pentane provided 42 mg (7%) of olefin (vide infra), followed by 59 mg of an oily mixture which was not identified; elution with ether–pentane (30:70) provided 477 mg (75%) of a mixture of alcohols III-α and III-β as a yellowish solid, mp 71–95°. Nmr analysis of this mixture showed it to be 50% III-α and 50% III-β.

An identical run provided 7% of the olefin, 55 mg of the unidentified mixture, and 76% of the alcohol mixture (mp 71–95°), which nmr analysis showed to be 50% III-α and 50% III-β.

The 4-vinyl[2.2]paracyclophane collected from the above runs was combined, rechromatographed, and crystallized from pentane to yield a white solid, mp 80–81°. The infrared spectrum showed a weak olefinic band at 6.15 μ. The nmr spectrum was as follows: ten protons (aromatic and vinyl) at τ 2.97–4.92 with the aromatic multiplet partially masking the vinyl absorption (similar to that of styrene),[23] and eight protons as a multiplet at τ 6.39–7.51 (bridge). *Anal.* Calcd for C$_{18}$H$_{18}$: C, 92.26; H, 7.74. Found: C, 92.10; H, 7.74.

Control Experiments for Hydrolysis of Trichloroacetates of 4-(1-Hydroxyethyl)-[2.2]paracyclophane. A solution of 254 mg (1.01 mmoles) of alcohol III-α and 164.5 mg (1.01 mmoles) of trichloroacetic acid in 100 ml of 9:1 dioxane–water (by volume) was held at 50° for 106 hr, then cooled, poured into 400 ml of water, and extracted four times with 175-ml portions of 3:1 ether–pentane. The combined organic layers were washed with 5% aqueous sodium bicarbonate and water and dried. Solvent was removed under reduced pressure. The residue was a solid, mp 102–104°, which tlc [pentane–ether–methanol (65:30:5) solvent system] showed to contain a trace of olefin and a trace of β alcohol III-β in addition to the predominant component, α alcohol III-α. This solid was chromatographed over a short column of activated silica gel, and ether–pentane (30:70) eluted the alcohol, 209 mg (82%). This was shown by nmr analysis to be greater than 99% alcohol III-α and less than 1% III-β. It was determined by the use of known solutions that 1% of either component in the other was the limit of detectability by the nmr technique. This involved scanning the carbinyl methyl doublets at 50-cycle sweep width at high spectrum amplitude to detect the 1% component.

A solution of 260 mg (1.03 mmoles) of alcohol III-β and 168 mg (1.03 mmoles) of trichloroacetic acid in 100 ml of 9:1 dioxane–water was treated as described for III-α above. The crude product, mp 108–111°, was shown by tlc to contain a trace of olefin and a small amount of alcohol III-α in addition to the major component, β alcohol III-β. Chromatography, as above, yielded 241 mg (93%) of the alcohol, shown by nmr analysis to contain about 1% alcohol III-α and 99% III-β.

A solution of 150 mg (0.64 mmole) of 4-vinyl[2.2]paracyclophane and 104 mg (0.64 mmole) of trichloroacetic acid in 20 ml of 9:1 dioxane–water was held at 50° for 66 hr and worked up similarly to the manner just described. Evaporation of solvent left 121 mg (81%) of a yellowish solid, mp 79–80°, which tlc [pentane and pentane–ether–methanol (65:30:5) solvent systems] showed to be unchanged olefin free of any alcoholic products.

1-(2,5-Dimethylphenyl)ethanol. A solution of 5.0 g of 2,5-dimethylacetophenone (Eastman White Label) in 20 ml of anhydrous ether was reduced with 1 g of lithium aluminum hydride in 40 ml of ether, and the product was isolated in the usual way. Removal of solvent left 4.89 g of a colorless oil which was distilled at 123° (pot) (0.1 mm) to yield the desired alcohol,[24] n^{25}D 1.5256. *Anal.* Calcd for C$_{10}$H$_{14}$O: C, 79.96; H, 9.39. Found: C, 80.20; H, 9.35.

The infrared spectrum of this material showed hydroxyl absorption at 2.8 and 2.9 μ. The nmr spectrum was as follows: one proton as a broad singlet at τ 2.73 (6-proton), two protons as an unsymmetrical doublet ($J = 1.5$ cps) at τ 3.09 (3- and 4-protons), one proton as a quartet ($J = 6.5$ cps) at τ 5.08 (methine), one proton as a broad singlet at τ 6.94 (hydroxyl), three protons as a singlet at τ 7.73 (2 methyl), three protons as a singlet at τ 7.82 (5-methyl), and three protons as a doublet ($J = 6.5$ cps) at τ 8.68 (carbinyl methyl).

4-Thioacetomorpholido[2.2]paracyclophane. To 35 ml of freshly distilled morpholine were added 15.0 g (0.06 mole) of 4-acetyl-[2.2]paracyclophane and 4 g (0.12 mole) of sulfur powder. The mixture was refluxed for 113 hr, during which time yellow crystals formed. The reaction mixture was cooled; the crystals were crushed, and the mixture was poured into 75 ml of absolute ethanol in a vessel which was allowed to stand in the cold, producing 16.3 g (78%) of yellow crystals, mp 205–235°. This material was shown by tlc (1:1 ethyl acetate–cyclohexane solvent system) to be predominantly the desired thioacetomorpholide plus minor amounts of other materials. Crystallization of this substance from ethanol–chloroform gave light tan crystals, mp 244–245° dec. The infrared spectrum showed strong bands for the —C(=S)N< function at 6.72, 6.96, 7.27, and 8.99 μ.[25] *Anal.* Calcd for C$_{22}$H$_{25}$NOS: C, 75.17; H, 7.17; S, 9.12. Found: C, 75.34; H, 6.98; S, 9.37.

4-Carboxymethylene[2.2]paracyclophane (V). A solution of 2.0 g (5.8 mmoles) of thiomorpholide in 50 ml of glacial acetic acid and 100 ml of concentrated hydrochloric acid was refluxed for 48 hr, during which time white crystals began to appear. The mixture was cooled and poured into 300 ml of water to precipitate a solid which was filtered, washed with water, then dissolved in chloroform, and dried. Evaporation of the chloroform left 1.4 g (93%) of acid V as yellowish crystals. Crystallization of this material from ether or ether–pentane gave white needles, mp 210–212° (lit.[7] mp 210–210.2°). The infrared spectrum showed a carbonyl band at 5.84 μ.

When this reaction was run with significantly larger amounts of material, the product was usually isolated as brownish flakes. Purification was effected by charcoal treatments in hot glacial acetic acid, followed by crystallization. This led to acid of mp 212–214°.

4-Acetonyl[2.2]paracyclophane (VI). A. Reaction of Methyllithium with Acid V. To a dried flask with nitrogen atmosphere were added 60 ml of anhydrous diethyl ether and 0.63 g (2.4 mmoles) of acid V to produce a suspension. Then 6 ml of a 1 M solution of methyllithium in ether was slowly added, immediately producing a yellow precipitate. The mixture was refluxed for 25 min and then stirred at 25° for 2.5 days under nitrogen. Dilute hydrochloric acid was added, dissolving the yellow precipitate, and the ether layer was washed with dilute potassium hydroxide (0.11 g of acid V was recovered from this wash) and four times with water and dried. Solvent was removed to leave 0.44 g of a yellow oil which was chromatographed over 44 g of activated silica gel. Elution with ether–pentane (10:90) produced 0.21 g (33%) of the desired ketone VI; elution with ether produced 0.14 g of a yellow waxy solid (vide infra).

Ketone VI was sublimed at 80° (0.15 mm) to provide a white solid, mp 97.8–98.8°. The infrared spectrum showed a carbonyl band at 5.86 μ. The nmr spectrum was as follows: six protons (aromatic) as a multiplet at τ 3.17–3.75 and one proton (ortho) as a singlet at τ 3.83, ten protons as a multiplet at τ 6.12–

(23) See, for example, J. R. Dryer, "Applications of Absorption Spectroscopy of Organic Compounds," Prentice-Hall, Inc., Englewood Cliffs, N. J., 1965, p 106.

(24) A. Klages and R. Keil, *Ber.*, 36, 1639 (1903).
(25) K. Nakanishi, "Infrared Absorption Spectroscopy," Holden-Day, Inc., San Francisco, Calif., 1962, p 54.

7.42 (methylene) including the α-keto methylene protons as an apparent AB quartet centered at τ 6.55 and overlapping the bridge-methylene protons, and three protons as a singlet at τ 8.07 (methyl). *Anal.* Calcd for $C_{19}H_{20}O$: C, 86.32; H, 7.63. Found: C, 86.59; H, 7.60.

The yellow solid mentioned above was shown by tlc [ethyl acetate–cyclohexane (30:70)] to be primarily one component, contaminated with some apparently polymeric materials. That this main component was primarily tertiary alcohol was shown by the spectral data. The infrared spectrum showed hydroxyl absorption at 2.8 and 2.9 μ. The nmr spectrum was as follows: aromatic protons as a multiplet at τ 3.25–3.75 with the *ortho* proton as a singlet at τ 3.88, methylene protons as a multiplet at τ 6.32–7.82, hydroxyl proton as a broad singlet at τ 8.38, and methyl protons as a singlet at τ 8.92. This material was not investigated further.

B. Reaction of Acid Chloride or V with Dimethylcadmium. (This is a modification of the method of Cason.)[26] A Grignard reagent was prepared by bubbling gaseous methyl bromide through 500 ml of ether containing 5.39 g (0.22 g-atom) of magnesium turnings until the magnesium had all reacted. The reagent was then cooled to 0°, and 21.56 g (0.118 mole) of anhydrous cadmium chloride (dried overnight at 120°) was added as a solid. The mixture was refluxed for 30 min. Most of the ether was evaporated, and the remaining ether was evaporated in a stream of nitrogen, leaving a brownish sludge. Then 500 ml of dry benzene was added, and the mixture was stirred with a very strong mechanical stirrer.

Acid chloride of V was prepared by stirring 13.8 g (0.052 mole) of acid V overnight with 50 ml of thionyl chloride (taken from a fresh bottle and distilled immediately before use; old thionyl chloride leads to troublesome side reactions). The resulting yellow solution was evaporated at reduced pressure, and 50 ml of dry benzene was added. This solvent was evaporated at reduced pressure, and this procedure was repeated two additional times to remove the last traces of thionyl chloride. The product was a yellow solid which had a carbonyl band at 5.58 μ in the infrared; this solid was not further characterized but was used immediately.

The acid chloride was dissolved in a minimum amount of dry benzene and added rather rapidly at room temperature to the dimethylcadmium reagent with very efficient stirring. A tan sludge formed immediately. The reaction mixture was stirred for 1 hr at 25° (heating leads to side reactions), then cooled in an ice bath and very carefully hydrolyzed with 2 N sulfuric acid. The aqueous layer was separated and extracted with ether, which was added to the benzene layer. The resulting solution was washed with water, 5% sodium bicarbonate (this wash yielded 108 mg of acid V), water, and saturated aqueous sodium chloride, and dried; solvent was evaporated to leave 14.8 g of a yellowish solid which tlc (1:1 ethyl acetate–cyclohexane solvent system) indicated to be primarily ketone VI with a small amount of tertiary alcohol and some polymeric materials. The product was chromatographed over 1400 g of activated silica gel which had been slurry packed in ether–pentane (5:95). Elution with this solvent and with ether–pentane 10:90 produced nothing; elution with ether–pentane 15:85 provided 11.5 g (83%) of ketone VI, mp 98–99°. The chromatography was discontinued.

4-(2-Deuterio-2-hydroxypropyl)-[2.2]paracyclophane (IV). A solution of 44.4 g (0.168 mole) of ketone VI in 1300 ml of anhydrous ether was added dropwise to a slurry of 5.86 g (0.14 mole) of lithium aluminum deuteride in 400 ml of ether under nitrogen atmosphere. The mixture was stirred overnight and then hydrolyzed by careful addition of 250 ml of saturated aqueous magnesium sulfate. The aqueous layer was separated and extracted three times with 3:1 ether–pentane. The combined organic layers were washed three times with water and dried. Evaporation of solvent left 44.6 g of alcohol IV as a white solid (mixture of diastereomers), mp 75–88°. The infrared spectrum showed hydroxyl absorption at 2.8 and 2.9 μ. *Anal.* Calcd for $C_{19}H_{21}DO$:[27] C, 85.35; H and D, 8.66. Found: C, 85.56; H and D, 8.54. (See a later part in the Experimental Section for the properties of IV-α and IV-β.)

Acetate of 4-(2-Deuterio-2-hydroxypropyl)-[2.2]paracyclophane and Separation into Diastereomers. To a solution of 10.00 g (0.0377 mole) of alcohol IV in 40 ml of dry pyridine was added a

solution of 7.5 ml (*ca.* 0.1 mole) of freshly distilled acetic anhydride in 10 ml of dry pyridine. The resulting solution was refluxed for 2 hr, cooled, and poured into 250 ml of 3:1 ether–pentane. This mixture was washed with 5% hydrochloric acid (three 200-ml portions), water, 5% sodium bicarbonate (two 50-ml portions), and water, and dried. Solvent was removed at reduced pressure to leave 11.4 g (98%) of acetate (mixture of diastereomers) as a white solid, mp 54–59°. *Anal.* Calcd for $C_{21}H_{23}DO_2$: C, 81.52; H and D, 8.58. Found: C, 81.56; H and D, 8.34.

Tlc [ether–pentane (25:75) solvent system] resolved this mixture into two closely spaced spots. The infrared spectrum showed a carbonyl band at 5.80 μ and ether stretching at 7.90 and 8.25 μ (shoulder). Nmr analysis (*vide infra*) showed the mixture to be 56–58% acetate of IV-α and 42–44% acetate IV-β.

A 5.00-g portion of the above mixture was chromatographed over 1100 g of activated silica gel which had been slurry packed in ether–pentane (10:90). Elution with 5.1 l. of this solvent produced only traces of material; the next 1.1 l. brought 2.31 g of pure acetate of IV-α; 0.3 l. brought 0.39 g of material which was a mixture of acetates of IV-α and IV-β; 0.2 l. brought 0.42 g of a mixture of the two acetates which was greatly enriched in β isomer; the next 2.2 l. brought 1.52 g of pure β-acetate.

Several other similar chromatographs were run until 11 g of pure α isomer had been collected; the material which was enriched in β isomer was crystallized from pentane–ether and added to the pure β isomer collected, giving 8.2 g.

The acetate of IV-α was crystallized from pentane–ether to give white flakes, mp 58.7–60.0°. The infrared spectrum showed a carbonyl band at 5.80 μ and ether stretching frequencies at 7.9 and 8.25 μ (shoulder). The nmr spectrum was as follows: seven protons (aromatic) as a multiplet at τ 3.24–4.00, including the *ortho* proton as a broadened singlet at τ 3.95, ten protons as a multiplet at τ 6.25–7.90 (methylene), three protons as a singlet at τ 8.04 (acetoxy methyl), and three protons as a singlet at τ 9.02 (carbinyl methyl).

The acetate of IV-β was crystallized from pentane–ether to give white flakes, mp 89.0–89.8°. The infrared spectrum was identical with that of the α isomer. The nmr spectrum of the β isomer was as follows: seven protons (aromatic) as a multiplet at τ 3.26–3.90, including the *ortho* proton as a broadened singlet at τ 3.85, ten protons as a multiplet at τ 6.53–7.45 (methylene), three protons as a singlet at τ 8.07 (acetoxy methyl), and three protons as a singlet at τ 8.94 (carbinyl methyl).

Diastereomers of 4-(2-Deuterio-2-hydroxypropyl)-[2.2]paracyclophane (IV-α and IV-β). A solution of 8.14 g (0.0263 mole) of α-acetate in 300 ml of ether was reduced in the usual way with 1.5 g of lithium aluminum hydride to give 6.98 g (94%) of IV-α. Crystallization from ether–pentane yielded white flakes, mp 120–121°. The infrared spectrum showed hydroxyl bands at 2.8 and 2.9 μ. The nmr spectrum was as follows: seven protons (aromatic) as a multiplet at τ 3.27–4.00, including the *ortho* proton as a broadened singlet at τ 3.92, ten protons as a multiplet at τ 6.36–7.88 (methylene), one proton as a broad singlet at τ 8.17 (hydroxyl), and three protons as a singlet at τ 8.96 (methyl).

Similar reduction of 5.90 g (0.0191 mole) of acetate of IV-β in 300 ml of ether with 1.1 g of lithium aluminum hydride produced, after work-up, 5.10 g (95%) of alcohol IV-β. Crystallization of this compound from ether–pentane yielded white flakes, mp 88.7–89.3°. The infrared spectrum showed hydroxyl bands at 2.8 and 2.9 μ. The nmr spectrum was as follows: seven protons (aromatic) as a multiplet at τ 3.23–3.97, including the *ortho* proton as a broadened singlet at τ 3.92, ten protons as a multiplet at τ 6.35–7.94 (methylene), one proton as a broad singlet at τ 8.28 (hydroxyl), and three protons as a singlet at τ 8.93 (methyl).

Tosylates of 4-(2-Deuterio-2-hydroxypropyl)-[2.2]paracyclophane (of IV-α and IV-β). A 5.50-g sample (0.020 mole) of alcohol IV-α was dissolved in 33 ml of dry pyridine, and the solution was cooled to 0°. Solid *p*-toluenesulfonyl chloride (4.20 g, 0.022 mole) was added, and the mixture was swirled until all the chloride had dissolved. The solution was kept at 0° for 24 hr, during which time large crystals of pyridine hydrochloride formed. The reaction mixture was poured into water and extracted three times with 3:1 ether–pentane. The combined extracts were washed with water, ice-cold 2 N sulfuric acid, 5% sodium bicarbonate, and water and dried. The solvent was concentrated to about 75 ml, diluted with an equal volume of pentane, again concentrated to about 75 ml, and allowed to stand at −18°. A clear oil separated; after several days this oil solidified to produce 6.71 g (78%) of white needles of tosylate of IV-α. This material was recrystallized from pentane–ether to give white needles which decomposed at 100–101°. The

(26) J. Cason, *J. Am. Chem. Soc.*, **68**, 2078 (1946).

(27) The lithium aluminum deuteride used in this reduction was 97–98% fully deuterated. No protio compound could be found in the product by nmr analysis, leading to the conclusion that the alcohols contained 97% or more of one atom of deuterium per molecule at the appropriate carbon atom.

infrared spectrum showed strong bands at 7.34 μ (antisymmetric SO_2)[25] and 8.49 μ (symmetric SO_2).[25] *Anal.* Calcd for $C_{26}H_{27}$-DO_3S: C, 74.07; H and D, 6.93. Found: C, 74.29; H and D, 7.05.

By the procedure just described, 4.50 g (0.0164 mole) of alcohol IV-β in 27 ml of dry pyridine was allowed to react at 0° with 3.44 g (0.0180 mole) of p-toluenesulfonyl chloride. After similar work-up, the solvent was concentrated to about 50 ml, diluted with an equal volume of pentane, again concentrated to about 50 ml, and allowed to stand at −18°. A clear oil separated; this oil slowly crystallized to form 4.44 g (63%) of tosylate of IV-β as fine white needles. This material was recrystallized from pentane–ether to give white needles, mp 95.8–96.5° (dec *ca.* 120°). The infrared spectrum of this material was identical with that of tosylate of IV-α above. *Anal.* Calcd for $C_{26}H_{27}DO_3S$: C, 74.07; H and D, 6.93. Found: C, 73.94; H and D, 6.98.

Kinetics of Acetolysis of Tosylates of 4-(2-Deuterio-2-hydroxy-propyl)-[2.2]paracyclophane (of IV-α and IV-β). Solutions of tosylates of IV-α and IV-β were prepared (0.010 M) by weighing the appropriate amounts of material into volumetric flasks and diluting to the mark with dry glacial acetic acid. Aliquots of 5 ml each were withdrawn with automatic pipets and sealed into clean ampoules. The ampoules were then placed in thermostated baths at the indicated temperatures, removed at the designated times, swirled in ice water for 1 min, and then stored at −20° until all tubes in a run could be titrated. The tubes were then opened and titrated to the light yellow end point of brom phenol blue (ten drops, saturated in glacial acetic acid)[28] indicator with 0.0113 M sodium acetate in dry glacial acetic acid (prepared by weighing 0.2987 g of dry, pure sodium carbonate into a 500-ml volumetric flask and diluting to the mark with dry glacial acetic acid).

The data were analyzed by a least-squares program on the IBM 7094 computer, and standard deviations are listed with the calculated first-order rate constants. The rate constants for two runs were averaged, along with their standard deviations, and thermodynamic functions (see Table I) were calculated in the usual way.

Table IV. Acetolysis of Tosylate of IV-α at 74.97 ± 0.06°

Series 1 NaOAc, ml	Time, min	Series 2 NaOAc, ml
0.240[a]	6.05	0.240[a]
0.480	12.24	0.480
0.700	18.20	0.700
0.935	25.05	0.950
1.180	32.09	1.180
1.360	38.02	1.340
1.575	45.26	1.565
1.800	54.14	1.805
1.990	63.02	2.010
2.260	75.07	2.270
3.155	135.02	3.150
4.190	(1182)	4.200
$k = 1.73 \pm 0.01$ $\times 10^{-4}\,\mathrm{sec}^{-1}$		$k = 1.72 \pm 0.01$ $\times 10^{-4}\,\mathrm{sec}^{-1}$
	Av $k = 1.72 \pm 0.01 \times 10^{-4}\,\mathrm{sec}^{-1}$	

[a] Not used in calculation of k.

Limits on these functions were determined, using the rate-constant standard deviations, by the method of total differentials.[22] Table IV records data from a typical run.

Acetolysis of Tosylates of 4-(2-Deuterio-2-hydroxypropyl)-[2.2]-paracyclophane (of IV-α and IV-β). A solution of 1.00 g (2.38 mmoles) of α-tosylate in 100 ml of dry glacial acetic acid was thermostated at 75° for 18 hr. The solution was cooled and shaken with a mixture of 200 ml of water and 100 ml of 1:1 ether–pentane. The aqueous layer was separated and extracted again with ether–pentane. The organic layers were combined, washed with two 100-ml portions of water, and dried. Solvent was evaporated at reduced pressure to leave an oil which was chromatographed over a short column of activated silica gel. Elution of the column with ether–pentane (0.5:99.5) produced 20 mg (3.4%) of a white solid which appeared by melting point (71–75°) and infrared to be a mixture of olefins but was not further characterized; elution with

ether–pentane (5:95) produced 674 mg (91.9%) of a mixture of acetates of IV-α and IV-β as an oil which gradually became a white solid. Nmr analysis of this mixture showed it to be 97.4% acetate of IV-α and 2.6% acetate of IV-β. This material was crystallized from pentane–ether to yield acetate of IV-α, mp 57–58.5°. Mixture melting point with an authentic sample gave mp 58–59.5°.

A solution of 1.00 g (2.38 mmoles) of the β-tosylate in 100 ml of dry glacial acetic acid was treated exactly as described above. Chromatography as described yielded 28 mg (4.7%) of the olefin mixture previously mentioned, followed by 663 mg (90.5%) of a mixture of acetates as a white solid. Nmr analysis showed this mixture to be 7.2% α-acetate and 92.8% β-acetate. This material was crystallized from pentane–ether to yield acetate of IV-β, mp 88–89°. Mixture melting point with authentic material gave mp 88–90°.

Control Experiments for Acetolysis Reactions of Tosylates of 4-(2-Deuterio-2-hydroxypropyl)-[2.2]paracyclophane. To 10 ml of dry glacial acetic acid were added 125 mg (0.405 mmole) of α-acetate and 70 mg (0.405 mmole) of anhydrous p-toluenesulfonic acid. The solution was kept at 75° for 18 hr and worked up as described for the acetolysis reactions (*vide supra*). Removal of solvent at reduced pressure left 130 mg of a clear, slightly yellow oil in which tlc [ether–pentane (20:80) solvent system] detected only α-acetate. Nmr analysis of this material showed it to be greater than 99% α-acetate and less than 1% β-acetate.

An analogous treatment was carried out with 125 mg of β-acetate. The product was 133 mg of a yellowish solid in which tlc detected only β-acetate. Nmr analysis of this material showed 1% or less of α-acetate and 99% or more of β-acetate.

Formolysis of Tosylates of 4-(2-Deuterio-2-hydroxypropyl)-[2.2]paracyclophane (of IV-α and IV-β). A 0.025 M solution of sodium formate in formic acid was prepared by adding 132 mg (1.25 mmoles) of dry, pure sodium carbonate to 100 ml of dry formic acid. Then 1.00 g (2.38 mmoles) of α-tosylate was added, and the mixture was thermostated at 75°. The tosylate dissolved in about 30 min. After 7 hr, the reaction mixture was cooled and shaken with a mixture of 200 ml of water and 100 ml of 3:1 ether–pentane. The aqueous layer was separated and extracted with another portion of 3:1 ether–pentane. The organic layers were combined, washed with two 100-ml portions of water, and dried. The solution was filtered, and 1 g of lithium aluminum hydride was added in small portions. The mixture was stirred overnight and then carefully hydrolyzed with saturated aqueous magnesium sulfate. The ether layer was decanted, and the aqueous layer was extracted with another portion of ether. The ether layers were combined, washed twice with water, and dried. Solvent was evaporated to leave the alcohol as a white solid. This material was dissolved in 5 ml of dry pyridine; 1 ml of freshly distilled acetic anhydride was added, and the solution was refluxed for 3 hr. The reaction mixture was worked up as described for the acetylation of alcohol IV (*vide supra*). The residue was chromatographed over a short column of activated silica gel. Elution with ether–pentane (3:97) afforded 557 mg (76.0%) of acetate as a clear oil which slowly became a white solid. Tlc [ether–pentane (20:80)] detected only acetate of IV-α in this material. Nmr analysis of this acetate showed it to be greater than 99% α-acetate and less than 1% β-acetate. Crystallization from pentane–ether yielded α-acetate as a white solid, mp 57–59°. Mixture melting point with authentic α-acetate gave mp 57–59°.

Tosylate of IV-β was treated in a manner exactly analogous to that described for the α-tosylate. After reduction of the formate to the alcohol and acetylation, the product was chromatographed over a short column of activated silica gel. Elution of the column with ether–pentane (3:97) provided 567 mg (78.3%) of acetate in which tlc detected only β-acetate. Nmr analysis showed this material to be less than 1% α-acetate and greater than 99% β-acetate. This substance was crystallized from pentane–ether to yield a white solid, mp 89–90°. Mixture melting point with authentic β-acetate gave mp 88.5–90°.

Nmr Analysis. All nmr spectral analyses were carried out on a Varian Associates Model A-60 analytical spectrophotometer. Solutions were approximately 2 M in deuteriochloroform as solvent (unless otherwise indicated) with tetramethylsilane as internal standard. Peak areas were measured by integration, allowing the total integral to be equal to the theoretical proton content in the molecule. In the spectra of alcohols, the nmr solutions were shaken with deuterium oxide to exchange the hydroxyl protons.

A. **Analysis of Products of Hydrolysis and Methanolysis of Trichloroacetates (of III-α, and III-β).** The relative amounts of alcohols III-α and III-β or of their ethers in a given mixture were de-

(28) S. Winstein, E. Grunwald, and L. L. Ingraham, *J. Am. Chem. Soc.*, 70, 821 (1948).

termined by integration of their carbinyl methyl doublets. In a given derivative these doublets were completely separated. The integration of each doublet was made ten times and averaged; the amount of each component was then calculated as a percentage of the total. In the case of alcohols III-α and III-β, the nmr solutions were shaken with deuterium oxide to exchange the hydroxyl protons so that the signals from these protons would not interfere with the comparison of the carbinyl methyl signals.

B. Analysis of Products of Acetolysis and Formolysis of Tosylates of IV-α and IV-β. The carbinyl methyl signals in the nmr spectra of the acetate products of the acetolysis reactions and of the derived acetates from the formolysis reactions were used as the indicator in determining the relative amounts of each component (when the percentage of one acetate in a mixture of the two was low, i.e., 10% or less, the acetoxy methyl signals were of no value in this determination). Base line was not reached between the carbinyl methyl signals so that relative integration was impossible. This necessitated the use of the method[29] which is described below.

Four solutions ranging from 1.0% α-acetate and 99.0% β-acetate to 10.0% α-acetate and 90.0% β-acetate and four solutions ranging from 90.0% α-acetate and 10.0% β-acetate to 99.0% α-acetate and 1.0% β-acetate were prepared. The carbinyl methyl signals in a given solution were then scanned ten times at 50-cycle sweep width, and the height of each of the two peaks was measured for each scan. Then the contribution of the lesser component to the total peak height of the two components was calculated (in per cent). This percentage was then plotted as a function of the known percentage of the lesser component in the mixture. The curve thus obtained was used to determine the relative amount of each acetate in the product from a solvolysis reaction. The results are estimated to be accurate to within ±0.5%. This method was useful in determining the presence of as little as 1% of one acetate in a mixture of the two.

Electrophilic Substitution at Saturated Carbon. XXXIII. The Stereochemical Fate of the α-Sulfonylcarbanion in Which Both Anion and Sulfone Groups Are Incorporated in Five-Membered Ring Systems[1]

Donald J. Cram and Thomas A. Whitney[2]

Contribution No. 1999 from The Department of Chemistry of The University of California at Los Angeles, Los Angeles, California 90024. Received April 3, 1967

Abstract: The stereochemical fate of the α-sulfonylcarbanion in which both anion and sulfone groups are incorporated in five-membered ring systems has been examined. The base-catalyzed decarboxylations of (−)-2-methyl-2,3-dihydrobenzothiophene-2-carboxylic acid 1-dioxide ((−)-I) to give 2-methyl-2,3-dihydrobenzothiophene 1-dioxide (II) and of (+)-2-methyltetrahydrothiophene-2-carboxylic acid 1-dioxide ((+)-III) to give 2-methyl-tetrahydrothiophene 1-dioxide (IV) were carried out. Optically pure (+)-II was prepared by fractional crystallization of material obtained by decarboxylation of (−)-I (in water buffered with ammonium acetate). Similarly, optically pure (−)-II-d was prepared from (+)-I (in buffered deuterium oxide). That optical purity of II was reached was demonstrated by an isotopic dilution–reresolution experiment. Optically pure (+)-IV was prepared by decarboxylation of one of the four optically pure stereoisomers of 5-methyltetrahydrothiophene-2-carboxylic acid 1-dioxide (V). Values of k_e/k_α (one-point rate constant for isotopic exchange over that for racemization) for base-catalyzed reaction of optically active II in various media were determined. Results were as follows: (+)-II-d in 91% dimethyl sulfoxide–9% methanol–potassium methoxide at 25° gave k_e/k_α = 0.64; (−)-II-d in 70% t-butyl alcohol–30% tetrahydrofuran–potassium t-butoxide at 25° gave k_e/k_α = 0.66; (−)-II-d in methanol–potassium methoxide at 76° gave k_e/k_α = 0.64; (+)-II-h in methanol-O-d–potassium methoxide at 76° gave k_e/k_α = 0.65. These isotopic exchange reactions occurred with considerable net inversion of configuration. In the run made in t-butyl alcohol–tetrahydrofuran, the partially racemized product was reresolved, and the deuterium content of each enantiomer determined. The kinetic isotope effect for racemization of optically active II under the same conditions was shown to be k^H/k^D = 1.3. From these data, the relative rates of three stereochemical processes were extracted: inversion without exchange, 1; net inversion with exchange, 3; racemization with exchange, 9. A conducted tour mechanism for the two inversion processes is formulated. In this mechanism, both carbanion and potassium ion (and ligand) rotations within contact ion pairs are envisioned as occurring without complete breaking of $C^- \cdots HOR$ hydrogen bonds. The stereochemical direction of decarboxylation of salts of (−)-I was studied. The product varied from (−)-II of 3% optical purity in t-butyl alcohol to (±)-II in dimethyl sulfoxide to (+)-II of 65% optical purity in water. An assignment of stereochemical course to these reactions is suggested based on the similarity between the pattern of results obtained in this and other systems. Decarboxylations of (+)-III gave IV with stereospecificities and solvent dependence similar to that observed with its benzo analog. In both the decarboxylations and isotopic exchange reactions, the results point to symmetrical (planar) α-sulfonylcarbanions in asymmetric environments as discrete reaction intermediates.

Unlike open-chain α-sulfonylcarbanions whose generation and proton capture proceeded with high retention of configuration,[3] the anion generated in the

base-catalyzed decarboxylation of optically active cyclic

(3) (a) D. J. Cram, W. D. Nielsen, and B. Rickborn, *J. Am. Chem.*

sulfone I was reported by Corey, *et al.*,[3e] to give "completely racemic sulfone" II. The authors concluded that the lack of stereospecificity of the reaction provided evidence for a planar cyclic α-sulfonylcarbanion as an intermediate in the reaction. In a large number of systems, we had previously shown that in most media planar carbanions were asymmetrically solvated and gave rise to optically active products.[4] Thus, the results of Corey, *et al.*, appeared anomalous and worthy of further scrutiny, particularly since neither the optically active starting materials nor optically active products were demonstrated to be optically stable under the conditions of the reactions.[5] Accordingly, we have reexamined the stereochemical course of the decarboxylation of I under a variety of conditions. Likewise, the decarboxylation of III to give IV has also been studied. However, the most important results of this paper concern the stereochemical course of the base-catalyzed hydrogen–deuterium exchange reaction between I and hydroxylic solvents.
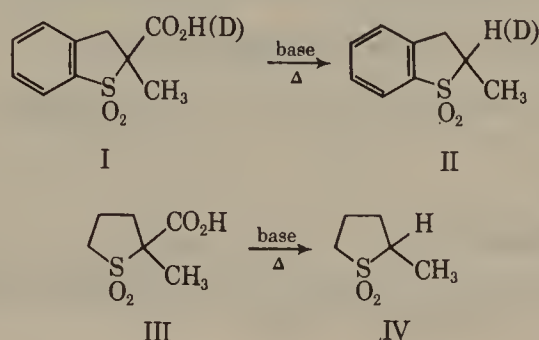
Results

Syntheses. Sulfone acid I was prepared by the sequence formulated. The substance was initially resolved through its brucine salt and brought to maximum rotation by recrystallization of the acid. Both enantiomers were obtained, (−)-I, $[\alpha]^{29}_{546}$ −83.9° (*c* 3, 95% ethanol), mp 169–171°, and (+)-I, $[\alpha]^{28}_{546}$ +80.5° (*c* 3, 95% ethanol), mp 168–170.5°, in reasonable overall yields.

Optically pure (−)-I was converted to its ammonium salt, which was submitted to decarboxylation at 155° in

Soc., **82**, 6415 (1960); (b) E. J. Corey and E. T. Kaiser, *ibid.*, **83**, 490 (1961); (c) D. J. Cram, D. A. Scott, and W. D. Nielsen, *ibid.*, **83**, 3696 (1961); (d) D. J. Cram and A. S. Wingrove, *ibid.*, **84**, 1496 (1962); **85**, 1100 (1963); (e) E. J. Corey, H. König, and T. H. Lowry, *Tetrahedron Letters*, 515 (1962); (f) E. J. Corey and T. H. Lowry, *ibid.*, 793, 803 (1965).

(4) For a summary, see D. J. Cram, "Fundamentals of Carbanion Chemistry," Academic Press Inc., New York, N. Y., 1965, pp 85–113 and 137–170.

(5) The following information regarding experimental details of the results reported in ref 3e has been provided by Professor E. J. Corey (private communication). Decarboxylation of optically active I was carried out by heating a homogeneous mixture of I and its pyridinium salt (initial ratio *ca.* 10:1) at 180–185° under vacuum (0.5 mm) so that the sulfone II was distilled from the reaction zone; the specific rotation of II in two runs was zero within experimental error (±0.5°) (work of H. König). In work subsequent to that reported in ref 3e (see T. H. Lowry, Ph.D. Thesis, Harvard University, 1964), the decarboxylation of I admixed with 0.09 equiv of potassium carbonate at 185° and under vacuum was carried out. "The product showed a small rotation ($[\alpha]$D +3.9° from acid $[\alpha]$D −77.8°) which could possibly have been due to an impurity but which could not be removed by various purification procedures" (quote from Lowry's thesis, p 43).

In our hands (D. J. C. and T. A. W.), repetition of the König experiment also gave racemic material. However, when the pure pyridinium salt of I was substituted for the 10:1 mixture of I and its pyridinium salt and the experiment repeated, (+)-II of rotation $[\alpha]^{25}_{546}$ +4.1° (*c* 4.6, CHCl₃) was produced [starting I was $[\alpha]^{25}_{546}$ −83.9° (*c* 3, C₂H₅OH)]. In our opinion, under the König conditions, most of the pyridine left the reaction zone, and the acid itself (not the salt) was the main species that underwent decarboxylation.

water containing enough acetic acid to provide a well-buffered solution at the end of the reaction. The (+)-II
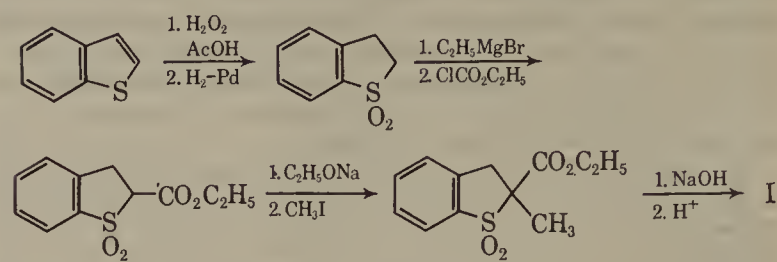
produced (54% optically pure) was crystallized to maximum rotation, $[\alpha]^{25}_{546}$ +24.1° (*c* 4, chloroform), mp 74–75°. Similarly, the ammonium salt N-*d*₄ of(+)-I was prepared and decarboxylated in deuterium oxide-deuterated acetic acid to give (−)-II-*d* (46% optically pure), which was recrystallized to maximum rotation, $[\alpha]^{25}_{546}$ −24.1° (*c* 4, chloroform), mp 73–74°, 98% of one atom of deuterium per molecule.[6a]

Since the validity of the conclusions of this paper depend on establishment of the rotation of optically pure II, an isotope dilution experiment was conducted.[7] A mixture of racemic II-*d* and active II-*h* was recrystallized until racemate and active II were separated, and each was analyzed for deuterium.[6b] From the rotations, the deuterium analyses, and the amounts of materials used, the maximum rotation of (±)-II was calculated to be $[\alpha]^{25}_{546}$ ±24.04 ± 0.4° (*c* 4, chloroform).

The synthesis of compound III is formulated. The substance was resolved through its brucine salt and brought to maximum rotation by repeated recrystallization of the acid itself, $[\alpha]^{25}_{546}$ +20.4° (*c* 4.7, water), mp 161.5–162.5°. The enantiomer was separated from racemate by fractional crystallization and brought to maximum rotation, $[\alpha]^{28}_{546}$ −20.2° (*c* 4.7, water), mp 159–160°.
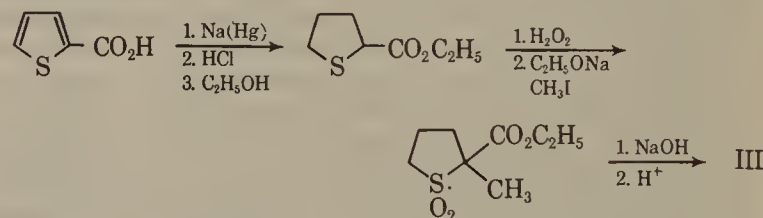
In order to establish the maximum rotation of optically active IV, one of the diastereomers of V was prepared (see reaction sequence). This material was resolved to maximum rotation through its brucine salt, followed by crystallization of the acid itself to maximum rotation, $[\alpha]^{26}_{546}$ +35.1° (*c* 4.9, chloroform), mp 78.5–80°. This material was subjected to base-catalyzed decarboxylation in buffered aqueous solution to give optically pure (+)-IV, $[\alpha]^{25}_{546}$ +11.80° (*c* 3.5, 95% ethanol). This decarboxylation was carried out
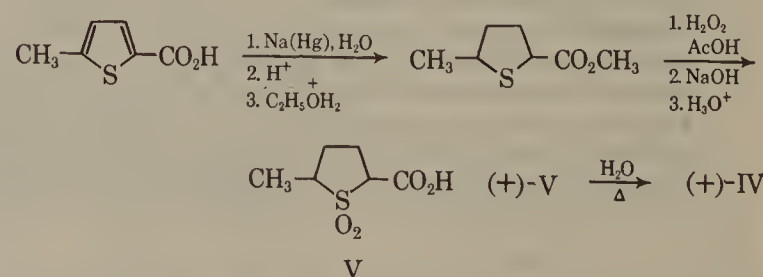
(6) (a) Combustion and falling drop method. (b) Mass spectral method.

(7) E. L. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, p 84.

Table I. Results of Exchange and Racemization of Optically Active 2-Methyl-2,3-dihydrobenzothiophene 1-Dioxide (II)

Run no.	Starting material Type	Concn, M	Solvent	Base Type	Concn, M	Temp, °C	Time, hr	% rac	% exch	k_e/k_α
1	II-d^a	0.33	$(CH_3)_2SO^b$	CH_3OK	0.16	25.0	72.0	42.0	31.0	0.64^c
2	II-d^a	0.33	$(CH_3)_3COH^d$	$(CH_3)_3COK$	0.028	25.0	1.08	56.8	42.7	0.66^c
3	II-d^a	0.164	CH_3OH	CH_3OK	0.16	76.2	11.5	64.6	48.7	0.64^c
4	II-h^e	0.164	CH_3OD^f	CH_3OK	0.16	76.2	9.75	84.5	70.0	0.65
5	II-d^a	0.059	$HOCH_2CH_2OH$	$HOCH_2CH_2OK$	0.059	76.2	143	43.7	34.5	0.73^c
6	II-h^e	0.10	$DOCH_2CH_2OD^g$	$DOCH_2CH_2OK$	0.10	76.2	76.0	78.2	65.5	0.70

[a] 97.7% of one atom of deuterium per molecule, $[\alpha]^{25}_{546}$ −24.1° (c 3.98, chloroform). [b] Solvent system: $(CH_3)_2SO$–CH_3OH, 93:7 by weight, 2.3 M in CH_3OH. [c] Corrected to 100% initial deuterium for substrate. [d] Solvent system: $(CH_3)_3COH$–tetrahydrofuran, 70:30 by volume. [e] $[\alpha]^{25}_{546}$ +24.1° (c 4.05, chloroform). [f] 99% of one atom of deuterium per molecule, combustion and falling drop. [g] 1.98 atoms of deuterium per molecule, combustion and falling drop.

under conditions that both starting material and product once formed retained their optical purities.

Base-Catalyzed Hydrogen Isotopic Exchange and Racemization of Sulfone II. Optically pure (+)-II-h and (−)-II-d were subjected to base-catalyzed hydrogen–deuterium exchange and racemization experiments, and the results are summarized in Table I. One-point, pseudo-first-order rate constants for isotope exchange of II with the medium (k_e) and for racemization of II (k_α) were calculated, and the ratios of k_e/k_α are listed. No base loss was observed in representative runs where the medium was titrated after reaction.

A deeper probe of mechanism was made of the exchange racemization of (−)-II-d in t-butyl alcohol–potassium t-butoxide. Thus, a 1.215-g portion of optically pure (−)-II-d was subjected to the same conditions as run 2 until 60% racemization had occurred. The substance was isolated and fractionally crystallized from ether into 99 ± 1% racemic II which contained 0.395 atom of deuterium per molecule,[6b] and optically pure (−)-II which contained 0.700 atom of deuterium per molecule. From these data, the isotopic composition of the (+)-II in the racemate is calculated to be 0.09 atom of deuterium per molecule. This calculation involves the assumption that the (−)-II fraction of the racemate has the same deuterium content as recovered pure (−)-II. The validity of this assumption was demonstrated by the fact that the same rotation for optically pure II was obtained from the isotopic dilution experiment as from crystallization of II to maximum rotation.[8] Furthermore, deuterium in excess of theory was not observed in either recovered racemate or antipode. Over-all racemization was 60% complete. Therefore, under the conditions of run 2, deuterium–hydrogen exchange of (−)-II-d in t-butyl alcohol proceeded with 2.7% isoinversion (inversion without exchange), 27.3% inversion with exchange, and 21% retention with exchange, while 49% of the starting material did not change. Combination of exchange with inversion and exchange with retention gives exchange with racemization, which amounts to 42 and 6.3% net exchange with inversion. The values for the stereospecific portions of the reaction are minimal since the products of initial exchange underwent further reaction.

The rate constants for racemization of (+)-II-h

(8) That deuterium- or hydrogen-labeled compound could be enriched by fractional crystallization of ±II and (−)-II would require that the crystal lattices of either racemate or enantiomer distinguish between deuterated and protonated material. Such discrimination is highly unlikely in view of the frequent inability of lattices to distinguish between much grosser structural features (e.g., a methyl or a bromine).

and (−)-II-d were carefully measured (13 points taken over the first 75% of the reaction) at 25° under the conditions of run 2, and were as follows: k_α^H = 2.90 ± 0.003 × 10^{-4} sec⁻¹; k_α^D = 2.24 ± 0.016 × 10^{-4} sec⁻¹; $(k^H/k^D)_\alpha$ = 1.29 ± 0.02. Application of the kinetic equations reported previously[9] to the above data provided the following approximate rate constants (× 10^{-4} sec⁻¹) at time zero: isoinversion, 0.138; net inversion with exchange, 0.42; racemization with exchange, 1.20.

Steric Course of the Decarboxylation Reactions. Decarboxylation experiments on optically pure (−)-I were carried out in a variety of solvents in the presence of a sufficient amount of base to produce catalysis, but not enough to racemize the product once formed. Table II reports the conditions of each run and the results. In all runs except 8 and 9, either less than 1 equiv of base (ammonium salt of (−)-I or potassium carbonate) was used, or the reaction medium itself was acidic (acetic acid, phenol, or buffered solutions). The decarboxylation media in runs employing less than 1 equiv of base were terminated before all free (−)-I had been consumed. The fact that II was produced with the same rotation in runs 8 and 9, even though the reaction times differed by a factor of 4, points to the optical stability of II once formed under the reaction conditions. Addition of optically active (+)-II to a decarboxylation run identical with run 15 gave results that demonstrated active II to be optically stable to the conditions of run 15. Examination of the rotation of recovered (−)-I from runs 15 and 19 demonstrated this acid to be optically stable under conditions of its decarboxylation. In the absence of base (−)-I was found not to decarboxylate in t-butyl alcohol or dimethyl sulfoxide at the temperatures of runs 15 and 19, respectively.

Decarboxylation experiments were also carried out on optically pure (+)-2-methyltetrahydrothiophene-2-carboxylic acid 1-dioxide ((+)-III) in water and t-butyl alcohol at 165°. Table III records the results. The ammonium or potassium salts of (+)-III served as the basic catalyst, and the reactions were terminated while free (+)-III was still present. A control run established that (+)-IV was optically stable under the conditions of run 24. Examination of the optical purity of recovered ammonium salt of (+)-III from run 23 established that (+)-III is optically stable under these conditions. Appropriate experiments established the

(9) W. T. Ford, E. W. Graham, and D. J. Cram, J. Am. Chem. Soc., 89, 689, 690 (1967).

Table II. Results of Base-Catalyzed Decarboxylation of (−)-2-Methyl-2,3-dihydrobenzothiophene-2-carboxylic Acid 1-Dioxide[a] ((−)-I)

Run no.	Solvent	Base Nature	Concn, N	Subst concn, N	Time, hr	Temp, °C	% react.	$[\alpha]^{25}_{546}$ of product,[b] deg	Net steric course,[c] %
7	None	$NH_4O_2CR^d$	...	...	0.28	185	79[e]	+5.03	21, inv
8	$HOCH_2CH_2OH$	$NH_4O_2CR^d$	0.178	0.178	0.50	165	77[f]	+10.06	41, inv
9	$HOCH_2CH_2OH$	$NH_4O_2CR^d$	0.178	0.178	2.0	165	93[f]	+10.07	41, inv
10	H_2O	$NH_4O_2CR^d$	0.0275	0.133	16.0	164	57[f]	+14.08	58, inv
11	H_2O	$KAPH^g$	0.05	0.067	36.0	164	98[f]	+14.10	58, inv
12	H_2O	$KAPH^{g,h}$	0.05	0.067	36.0	164	92[f]	+13.10	54, inv
13	H_2O	NH_4OAc	0.266	0.133	48.0	155	95[f]	+14.10	58, inv
14	H_2O	$KAPH^g$	0.05	0.067	815	103	16[f]	+15.60	64, inv
15	$(CH_3)_3COH$	$NH_4O_2CR^d$	0.0133	0.123	14.0	164	35[e]	−0.75	3.1, ret
16	CH_3CO_2H	KO_2CR^i	0.397	0.133	43.5	200	94[f]	+4.73	20, inv
17	CH_3CO_2H	KO_2CR^i	0.512	0.133	120	164	92[f]	+5.22	22, inv
18	C_6H_5OH	$NH_4O_2CR^d$	0.133	0.133	24.0	200	86[f]	+4.67	19, inv
19	$(CH_3)_2SO$	$NH_4O_2CR^d$	0.0133	0.150	1.25	142	55[f]	0.0	100, rac
20	D_2O	$ND_4O_2CR^{i,k}$	5.41	5.41	48.0	155	98[f]	−11.0	45.5, inv
21	H_2O	$NH_4O_2CR^{d,l}$	5.48	5.48	48.0	155	95[f]	+13.23	54.5, inv

[a] $[\alpha]^{25}_{546}$ −83.9° (c 3, 95% ethanol). [b] c 4, chloroform. [c] Based on +24.2° for (+)-II. [d] Ammonium salt of (−)-I. [e] Based on weight of recovered starting material. [f] Based on product isolated. [g] Potassium acid phthalate. [h] 5.37 M in potassium chloride. [i] Potassium salt of (−)-I. [j] Ammonium salt N-d_4 of (+)-I. [k] 6.18 M in acetic acid-O-d. [l] 5.65 M in acetic acid.

Table III. Base-Catalyzed Decarboxylation of (+)-2-Methyltetrahydrothiophene-2-carboxylic Acid 1-Dioxide[a] ((+)-III) at 165 ± 0.2°

Run no.	Solvent	Base Nature	Concn, N	Starting material concn, N	Time, hr	% react.[b]	$[\alpha]^{25}_{546}$ of product,[c] deg	Net steric course,[d] %
22	H_2O	KO_2CR^e	0.064	0.192	238	54	+5.31	45, inv
23	H_2O	$NH_4O_2CR^e$	0.064	0.192	236	45	+5.60	48, inv
24	$(CH_3)_3COH$	KO_2CR^e	0.064	0.192	8	68	0.0	100, rac
25	$(CH_3)_3COH$	$NH_4O_2CR^e$	0.064	0.192	14	61	+0.35	3, inv

[a] $[\alpha]^{25}_{546}$ +20.4° (c 4.71, water). [b] Based on weight of recovered starting material. [c] c 10, 95% ethanol. [d] Based on a maximum rotation of $[\alpha]^{25}_{546}$ +11.80° (c 4, 95% ethanol) for (+)-2-methyltetrahydrothiophene 1-dioxide. [e] Salts of (+)-III.

stability of (+)-III in the absence of base under the conditions of the decarboxylations.

Discussion

The following topics are discussed in turn: (1) the configuration of the cyclic α-sulfonylcarbanion; (2) the inversion mechanisms both with and without isotopic exchange (the conducted tour mechanism); and (3) the stereochemical courses for the decarboxylation reaction.

Configuration of the Cyclic α-Sulfonylcarbanion. The over-all stereochemical course of base-catalyzed hydrogen–deuterium exchange reactions can be determined by the values of k_e/k_α: values greater than 1 point to net retention; values equal to 1 indicate racemization; values between 0.5 and 1 indicate net inversion, either with or without isotopic exchange; and values of less than 0.5 point to a net isoinversion mechanism (net inversion without isotopic exchange). In a variety of solvents, optically active 2-phenylsulfonyl-2-octane (VI) underwent base-catalyzed isotopic exchange with values of k_e/k_α that ranged between 10 and ∼2000, depending mainly on medium.[3a,c] This result was contrasted with those obtained in systems which generated the 2-phenyl-2-butyl or the 1-methoxy-1-phenylethyl anions, in which nondissociating solvents gave $k_e/k_\alpha > 1$, dimethyl sulfoxide gave $k_e/k_\alpha = 1$, and protic dissociating solvents (such as diethylene glycol) gave $k_e/k_\alpha < 1$.[10] Since the latter

(10) D. J. Cram, C. A. Kingsbury, and B. Rickborn, *J. Am. Chem. Soc.*, 83, 3688 (1961).

systems in which phenyl served as the anion-stabilizing substituent were thought to generate planar or near-planar carbanions, the affinity of the open-chain sulfone system for a retention mechanism in all media was taken as evidence of an asymmetric carbanion. The asymmetry of the anion was attributed to either an electrostatically induced pyramidal anion whose inversion rate was less than that of proton capture, or to a planar carbanion in an asymmetric conformation whose formation and consumption for electrostatic reasons involved predominantly one particular face.[3a,c]

In the anion derived by proton abstraction from cyclic sulfone II, the ring system enforces a conformation which destroys the electrostatic driving force for generation of a pyramidal anion; the ring system also imposes symmetry on the anion if it is planar. Thus, it was anticipated that the pattern of k_e/k_α values obtained in cyclic system II would differ from those in VI, as indeed is observed. In all three types of solvents, k_e/k_α values are 0.64–0.73 (Table I). Thus, system II differs in behavior not only from its open-chain analog (VI), but also from the 2-phenyl-2-butyl anion, which gave $k_e/k_\alpha > 1$ in t-butyl alcohol–potassium t-butoxide. Indeed, the behavior of II is more similar to systems VII and VIII, which in t-butyl alcohol–tripropylamine

VII   VIII
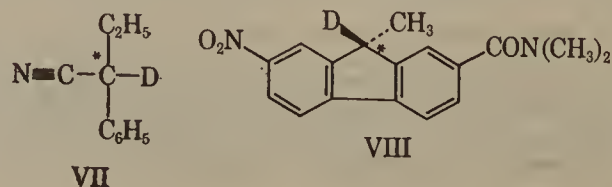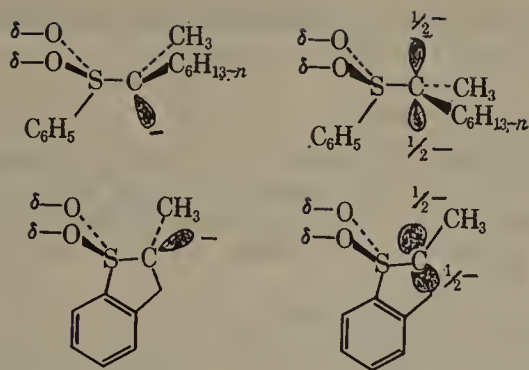
produced values of $k_e/k_\alpha < 1$.[11] The anions derived from VII and VIII are clearly close to planar, and on the basis of these comparisons, it seems very probable that the cyclic sulfonyl anion derived from II is also planar.[12]

Isoinversion and the Conducted Tour Mechanism for Intramolecular Proton Transfer. In t-butyl alcohol–potassium t-butoxide, $(-)$-II-d gave $k_e/k_\alpha = 0.66$, or exchange with net inversion (run 2). However, separate deuterium analysis of the $(-)$-II and $(+)$-II produced in the experiment revealed that this ratio reflected a blend of processes, whose relative rates were as follows: inversion without exchange (isoinversion), 1; net inversion with exchange, 3; racemization, 9. The simplest mechanism which provides an explanation of these facts is formulated in Chart I. In this scheme,

Chart I
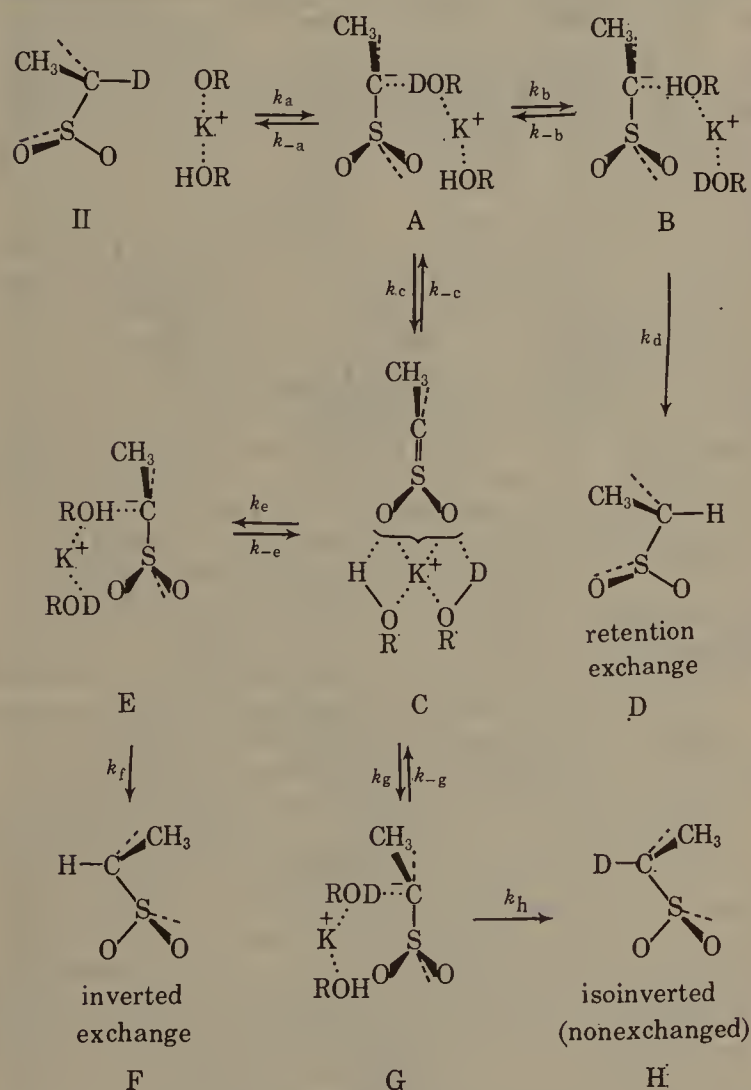
produced a covalent state gives isoinverted product, H.

potassium carbanide ion pair (A) in which the carbanion is hydrogen bonded to the deuterated t-butyl alcohol molecule formed by deuterium abstraction, the oxygen of which serves as a ligand to the potassium ion. Rotation of the potassium ion with its ligands provides B, collapse of which leads to exchanged product of retained configuration. Intermediate A can undergo a second reorganization reaction to produce C, in which the oxygens of the sulfone group serve as hydrogen-bonding sites and ligand centers for the potassium ion. Intermediate C can go to A, E, or G. In E, potassium ion with its deuterated and nondeuterated ligands has passed to the back face of the carbanion, and the nondeuterated ligand has become hydrogen bonded to the carbanion. Collapse of E leads to F, the inverted exchanged product. In G, the carbanion is hydrogen bonded at its back face with deuterated ligand. Collapse of G to the covalent state gives isoinverted product, H.

In a sense, the deuterium originally hydrogen bonded at the front face of the carbanion has gone on a *conducted tour* of hydrogen-bonding sites out around the two oxygens of the sulfone group and back to carbon on the opposite face. In the transition states for each stage of A → C → G, a hydrogen bond is made and broken, and the contact ion pair is preserved. Equal amounts of exchange with retention and exchange with inversion blend to give racemization with exchange, and this blend is not differentiable from stereochemically indiscriminant processes (*e.g.*, those involving ion-pair dissociation). However, the presence of an isoinversion process points also to the inversion and retention with exchange components as distinct stereospecific reactions. Indeed, the data require that exchange with inversion exceeds exchange with retention by a substantial amount. The results of this investigation of the stereochemical capabilities of the anion of II demonstrate the first unequivocable example of the rate of exchange with inversion exceeding the rate of exchange with retention. Clearly, an exchange with retention component must also be present.

The scheme of Chart I provides an explanation for the differences in behavior of sulfone II and 2-phenylbutane ($k_e/k_\alpha = 5$ to 10 in t-butyl alcohol–potassium t-butoxide).[10] Although both derived anions are planar, the 2-phenyl-2-butyl anion does not possess the essentially spherical array of hydrogen-bonding sites offered by the sulfone group for conducting protons from the front to the back face of the carbanion.

The net inversion observed in the other media (runs 1 and 3–6 of Table I) also probably reflects blends of isoinversion, inversion, and retention. However, a detailed discussion must await data on the distribution of deuterium between the enantiomeric components of partially racemized product.

The Kinetic Isotope Effect for Racemization of II. The kinetic isotope effect for racemization of optically active II in t-butyl alcohol–potassium t-butoxide was $(k^H/k^D)_\alpha = 1.29 \pm 0.02$ at 25°. This low isotope effect contrasts with the much higher kinetic isotope effects observed for hydrogen–deuterium exchange of toluene in cyclohexylamine–lithium cyclohexylamide,[13] (k^H/k^D) ~ 10, and of 2-N,N-dimethylcarboxamido-9-methyl-

potassium butoxide ion pair with its ligands of t-butyl alcohol detaches deuterium from substrate to form a

(11) D. J. Cram and L. Gosser, *J. Am. Chem. Soc.*, **86**, 2950, 5457 (1964).

(12) This same conclusion was drawn earlier by Corey, *et al.* (ref 3e), on the basis of equivocal experiments (see introductory section and ref 3).

(13) H. Streitwieser, W. C. Langworthy, and D. E. Van Sickle, *J. Am. Chem. Soc.*, **84**, 251 (1962).

fluorene[9] in methanol–potassium methoxide, $(k^H/k^D)_\alpha$ = 6. Particularly interesting is the fact that both the latter example[9] and the one of the current paper exhibited an isoinversion component, but rather different isotope effects. The low isotope effect for II in t-butyl alcohol–potassium t-butoxide points to k_{-a} (Chart I) being higher valued than k_b or k_c or any ion-pair dissociative process.[3c,10,14] Thus, the highest energy transition state for racemization does not involve covalent bond breaking but only a reorganization of hydrogen bonds. If the reaction described by k_{-a} is faster than such reorganization reactions, then the other covalent bond-making processes described by k_d, k_f, and k_h (Chart I) also must be faster. Thus, at the beginning of the reactions when products have not accumulated, the reverse reorganization processes described by k_{-b}, k_{-c}, k_{-e}, and k_{-g} must occur to very little extent.

The Stereochemistry of the Decarboxylation Reactions. The relative configurations of I and II have not been related by any means other than the decarboxylation reaction. Thus, an unequivocal assignment of relative configurations of I and II and of the stereochemical courses for the decarboxylations is not possible. However, several analogies exist which suggest tentative assignments for both. The stereochemical fates of carbanions generated with carbon or hydrogen as leaving groups have been similar to one another. Such has been the case for the 2-phenylsulfonyl-2-octyl,[3] the 2-phenyl-2-butyl, and the 1-methoxy-1-phenyl-1-ethyl carbanions.[15] The first of these anions is thought to be asymmetric and the last two symmetric. Furthermore, the patterns of dependence of the stereochemical results on medium are somewhat similar for the decarboxylations of I and the base-catalyzed cleavages leading to 2-phenylbutane or 1-methoxy-1-phenylethane. Thus, in dimethyl sulfoxide, the decarboxylation goes with total lack of stereospecificity (run 19 of Table II), in ethylene glycol with considerable stereospecificity in one direction (runs 8 and 9), but in t-butyl alcohol with low stereospecificity in the other direction (run 15). Cleavages of alcohols to give 2-phenylbutane and 1-methoxy-1-phenylethane go with total racemization in dimethyl sulfoxide, inversion in ethylene glycol, and retention in t-butyl alcohol.[16] Likely, the decarboxylations of II to give I follow a similar stereochemical course. Thus, dissociating protic solvents such as water and ethylene glycol give inversion, dissociating nonprotic solvents such as dimethyl sulfoxide produce racemization, and nondissociating solvents such as t-butyl alcohol lead to retention. The mechanisms underlying these stereochemical courses have been discussed previously, and need not be detailed here. It is striking that the solvent that provided the highest stereospecificity was water, and that lower temperatures produced the highest values (compare runs 12 and 14 of Table II). Also, water produced a substantially higher stereospecificity than deuterium oxide (compare runs 20 and 21). The same conclusions

drawn for the decarboxylation of I to II probably apply equally well for III to IV.

Experimental Section

All melting points were determined by the use of capillary tubes and are uncorrected. All temperatures are in degrees centigrade. Rotations were taken with a Zeiss circular polarimeter (tetrahydrothiophene system) or a Perkin-Elmer Model 141 polarimeter (dihydrobenzothiophene systems). The observed rotations were generally ±0.02° with the Zeiss instrument and ±0.005° with the Perkin-Elmer instrument. Infrared spectra were taken with a Beckman IR-5 spectrophotometer. Nuclear magnetic resonance spectra were taken with a Varian Associates A-60 spectrometer in deuteriochloroform with 2% tetramethylsilane as internal standard unless otherwise specified.

2-Carbethoxy-2,3-dihydrobenzothiophene 1-Dioxide. From 30.0 g of benzothiophene was prepared 24.1 g of benzothiophene 1-dioxide,[17a] mp 141.5–142.5° (lit.[17] mp 142–143°). This sulfone (15 g) was reduced to give 15 g of 2,3-dihydrobenzothiophene 1-dioxide,[17b] mp 90–91° (lit.[17b] mp 88–89°). A Grignard reagent was prepared from 11.2 g of magnesium, 55 g of ethyl bromide, and 480 ml of ether. To the rapidly stirred reagent was added dropwise a solution of 50 g of the sulfone in 350 ml of benzene. A white salt precipitated. When addition was complete, the reaction mixture was refluxed with stirring for 2 hr, and added in small portions to 260 g of freshly distilled ethyl chloroformate cooled in an ice bath and very rapidly stirred. The reaction mixture was refluxed for 18 hr and then filtered. The filter cake was extracted twice with 700-ml portions of chloroform. The extracts were combined with the filtrate and evaporated at reduced pressure, yielding 77 g of a viscous, brown oil. The crude product was not purified, but was used directly in the next step.

2-Methyl-2,3-dihydrobenzothiophene-2-carboxylic Acid 1-Dioxide (I). A sodium ethoxide solution was prepared from 70 g of sodium and 1400 ml of absolute ethyl alcohol. To the basic solution was slowly added a solution of 217 g of crude 2-carbethoxy-2,3-dihydrobenzothiophene 1-dioxide in 950 ml of absolute ethyl alcohol with rapid stirring while the temperature of the reaction mixture was maintained at 70°. The reaction mixture was stirred for 2 hr at 70°, then cooled to 20°; 560 g of methyl iodide was added dropwise, and the reaction mixture was reheated to 60° and stirred for 48 hr. Evaporation of ethanol under reduced pressure yielded a viscous, brown oil which was hydrolyzed in a hot solution of 60 g of sodium hydroxide in 1400 ml of water. Acidification of the hydrolysis reaction mixture with 100 ml of 96% sulfuric acid with ice bath cooling precipitated crude I as a yellow solid. This material was recrystallized from chloroform–methanol, weight 79.8 g (24.8% from 2,3-dihydrobenzothiophene 1-dioxide as colorless needles), mp 181–183°. This material exhibited strong infrared absorptions at 1750 cm^{-1}, characteristic of carboxylic acids, and at 1320 and 1160 cm^{-1}, characteristic of the sulfone group.[18] The nmr spectrum in DMSO-d_6 (tetramethylsilane as standard) showed the following absorptions: aromatic protons (multiplet, 4.0 protons), τ 2.0–2.6; benzyl protons (AB quartet, J_{AB} = 17 cps, ν = 27, 1.97 protons), centered at τ 6.45; methyl protons (singlet, 2.86 protons), τ 8.38. *Anal.* Calcd for $C_{10}H_{10}SO_4$: C, 53.09; H, 4.45; S, 14.17. Found: C, 53.27; H, 4.28; S, 14.44.

(−)-2-Methyl-2,3-dihydrobenzothiophene-2-carboxylic Acid 1-Dioxide ((−)-I). A solution of 169.7 g of I and 295.8 g of brucine in 1793 ml of refluxing 50:50 acetone–water was prepared. The flask containing the salt solution was sealed tightly and allowed to cool slowly to 25° in a large water bath, and the salt (137.7 g) separated as large plates. Recrystallization of the salt from 975 ml of the same solvent yielded 124.3 g (26.6%). A small portion of the salt was converted to the free acid which, after one crystallization from ether, exhibited $[\alpha]^{29}_{546}$ −83.9° (c 2.9 ethanol). Additional crystallizations of the salt provided no change in rotation of the derived acid after one crystallization from ether. The optically pure salt (132.3 g) was dissolved in 5000 ml of boiling water, and a solution of 66 g of potassium carbonate in 100 ml of water was added with rapid stirring. The solution was cooled to 0° for 1 hr to complete precipitation of brucine. The slurry was filtered, and the filtrate was reduced in volume to 400 ml under re-

(14) D. J. Cram, "Fundamentals of Carbanion Chemistry," Academic Press Inc., New York, N. Y., 1965, p 28.

(15) D. J. Cram, K. R. Kopecky, F. Hauck, and A. Langemann, *J. Am. Chem. Soc.*, 81, 5754 (1959), and ref 14, p 137.

(16) D. J. Cram, J. L. Mateos, F. Hauck, A. Langemann, K. R. Kopecky, W. D. Nielsen, and J. Allinger, *ibid.*, 81, 5774 (1959).

(17) (a) F. G. Bordwell, B. B. Lampert, and W. H. McKellin, *ibid.*, 71, 1704 (1949); (b) F. G. Bordwell and W. H. McKellin, *ibid.*, 72, 1986 (1950).

(18) K. Nakanishi, "Infrared Absorption Spectroscopy," Holden-Day, Inc., San Francisco, Calif., 1962, p 54.

duced pressure and filtered. Sulfuric acid, 130 ml, was added slowly to the concentrated filtrate with stirring and cooling, and crude (−)-I separated as an oil which was recovered by extraction with four 400-ml portions of chloroform. The combined extracts were dried and evaporated to dryness, yielding a white solid which was recrystallized from ether (26.8 g, 15.8% as large, colorless crystals), $[\alpha]^{29}_{546}$ −83.9° (c 2.9, ethanol), mp 169–171°; lit.[3e] $[\alpha]^{26}_{546}$ +59.0° (not given, ethanol), mp 161–162°; lit.[5] $[\alpha]^{27}_{546}$ −77.8° (c 1.8, 95% ethanol), mp 168–170.5°. *Anal.* Calcd for $C_{10}H_{10}SO_4$: C, 53.09; H, 4.45; S, 14.17. Found: C, 53.14; H, 4.50; S, 14.50.

(+)-2-Methyl-2,3-dihydrobenzothiophene-2-carboxylic Acid 1-Dioxide ((+)-I). To the mother liquor from the first crystallization of the brucine salt of I was added a solution of 60 g of potassium carbonate in 1000 ml of water with rapid stirring at 0°. The slurry was filtered, reduced in volume to 450 ml under reduced pressure, and filtered. Chloroform, 700 ml, was added to the basic solution; the solution was cooled in an ice bath and stirred rapidly, and 100 ml of 96% sulfuric acid was added slowly. The layers were separated, and the aqueous phase was extracted with three 430-ml portions of chloroform. The combined chloroform extract was dried and allowed to stand for 18 hr at 25°, whereupon 20.1 g of racemic I separated, mp 182–183°, $[\alpha]^{26}_{546}$ 0.0° (c 3.3, ethanol). The chloroform solution was evaporated to dryness under reduced pressure to give 57.0 g of crude (+)-I. This material was refluxed with 1000 ml of ether for 4 hr, and the solution was filtered, reduced in volume to 300 ml, cooled, and filtered again, thereby removing an additional 6.4 g of racemic I. Controlled evaporation of the filtrate yielded 28.1 g of crystalline (+)-I, mp 168–170.5°, $[\alpha]^{28}_{546}$ +80.5° (c 2.9, ethanol).

Ammonium Salt of (−)-2-Methyl-2,3-dihydrobenzothiophene-2-carboxylic Acid 1-Dioxide. A 4.0-g portion of optically pure (−)-I was dissolved in 150 ml of ether. Anhydrous ammonia gas was bubbled into the solution for 40 min, and the salt that separated as a white solid (4.2 g, 95%), was dried 4 hr under vacuum, $[\alpha]_{546}$ −61.0° (c 2.9, water).

Representative Decarboxylation of (−)-2-Methyl-2,3-dihydrobenzothiophene-2-carboxylic Acid 1-Dioxide ((−)-I) (Run 11). Optically pure (−)-I, $[\alpha]^{25}_{546}$ −83.9° (c 3.3, 95% ethanol), 0.300 g, was dissolved in 20 ml of 0.05 M potassium biphthalate buffer solution (pH 4.0) contained in a glass ampoule which had been previously purged with nitrogen. The ampoule was sealed and placed in a constant-temperature bath at 164° for 36 hr. The ampoule was opened; 30 ml of benzene was added, and the contents were thoroughly shaken before being transferred to a separatory funnel. The ampoule was rinsed twice with 10-ml portions of benzene which were added to the funnel. The layers were separated, and the aqueous phase was extracted once more with 20 ml of benzene. The combined organic phase was washed with a 30-ml portion of 3% aqueous sodium carbonate solution. The benzene solution of the product was filtered, evaporated to 20 ml on a hot plate, and finally evaporated to dryness on a rotary evaporator. The product, (+)-II (0.235 g, 98%), was chromatographed on a 1 × 30 cm column of silica gel with ether–pentane 40:60 as eluent, weight 0.221 g, $[\alpha]_{546}$ +14.10° (c 3.87, chloroform).

General Experimental Procedure for Base-Catalyzed Decarboxylation of (−)-2-Methyl-2,3-dihydrobenzothiophene-2-carboxylic Acid 1-Dioxide ((−)-I). The crude product from run 7 (100% ammonium salt of (−)-I, no solvent) was extracted with 20 ml of hot benzene, and the benzene extract was filtered. The filtrate was evaporated to dryness under vacuum, and the rotation of the product, (+)-II, was determined in chloroform after purification by chromatography on silica gel. Runs 8 and 9 were conducted as follows. Into each of two 1 × 20 cm test tubes was weighed 0.303 g of optically pure ammonium salt of (−)-I, and 7 ml of ethylene glycol was added. In run 8 the tube, open to the atmosphere, was heated in a constant-temperature bath at 165° for 0.5 hr; in run 9 the time of heating was 2.0 hr. The isolation procedure in both runs was the same. The decarboxylation reaction mixture was poured into 25 ml of ice water and extracted with two 25-ml portions of benzene. The combined extracts were washed with two 25-ml portions of water and evaporated to dryness under vacuum. The product was then chromatographed as in run 7.

Run 10 was conducted identically with that of run 11, except that 25 mole % ammonium salt of (−)-I was used as base, and isolation involved addition of ammonium carbonate to convert excess undecarboxylated acid to its ammonium salt (see below). The product, weight 0.165 g (57%), displayed $[\alpha]^{25}_{546}$ +14.08° (c 3.2, chloroform).

Run 12 was conducted identically with that of run 11, except that

8.0 g of potassium chloride was added to the decarboxylation reaction mixture before heating.

Run 13 employed 0.300 g of optically pure (−)-I and 0.205 g of ammonium acetate as base in 10 ml of water. Isolation was identical with run 11.

Run 14 was conducted identically with that of run 11, except that the reaction mixture was thermostated at 103°.

Run 15 employed 0.2767 g of (−)-I and 0.0324 g of the ammonium salt of (−)-I (both optically pure) as base (10 mole % base) in 10 ml of t-butyl alcohol. After heating, the solvent was removed under reduced pressure, 7 ml of water was added to the residue, and pH of the solution was found to be 3. Sufficient aqueous 10% ammonium carbonate solution was added to make the pH of the solution 8–9, and the product was recovered by benzene extraction and was purified as in run 11. To the aqueous phase was added 1 ml of 96% sulfuric acid and undecarboxylated (−)-I precipitated. The acid was recovered by two extractions with 40 ml of chloroform; the extracts were dried and evaporated, yielding 0.178 g of crude, recovered (−)-I, $[\alpha]^{25}_{546}$ −80.5° (c 3.34, 95% ethanol).

Run 16 was conducted as follows. A 0.300-g portion of optically pure (−)-I and 0.390 g of potassium acetate were placed in an ampoule. A 10-ml aliquot of glacial acetic acid was added to the ampoule with the aid of a syringe; the ampoule was purged with nitrogen, sealed, and placed in a constant-temperature bath at 200° for 43.5 hr. After this time, the tube was cooled, and the contents were removed. Evaporation of acetic acid left a viscous oil to which was added 7 ml of water and 7 ml of aqueous 20% potassium carbonate solution. The product was recovered and purified as in run 11, weight 0.223 g (94%), $[\alpha]^{25}_{546}$ +4.73° (c 3.9, chloroform).

Run 17 was conducted identically with that of run 16, except that 0.500 g of potassium acetate was used as base.

In run 18, a 300-mg portion of optically pure ammonium salt of (−)-I was placed in an ampoule, 10 ml of warm phenol was added, and the ampoule was purged with nitrogen and sealed. After standing in a constant-temperature bath at 200° for 24 hr, the ampoule was opened, and the contents were poured into 25 ml of water. A 30-ml portion of aqueous 15% sodium hydroxide solution, along with 50 ml of benzene, was added to the water. After thorough shaking, the layers were separated, and the aqueous phase was extracted with an additional 40-ml portion of benzene. The combined benzene extracts were washed with a 30-ml aliquot of aqueous 15% sodium hydroxide solution and twice with 30-ml volumes of water. Isolation and purification of the product were the same as in run 11.

In run 19, a 0.337-g portion of (−)-I and 0.0324 g of the ammonium salt of (−)-I (both optically pure) (8 mole % base) were placed in an ampoule, and 10 ml of dimethyl sulfoxide was added. The ampoule was purged with nitrogen, sealed, and placed in a constant-temperature bath at 142° for 75 min. The tube was opened and the contents removed. Evaporation of the solvent under reduced pressure left a semisolid to which was added 7 ml of water. The pH of the mixture was 2–3. Potassium carbonate solution was added to the acidic mixture until the pH became 8–9 and the product was recovered and purified as in run 11, weight 0.150 g (55%), $[\alpha]^{25}_{546}$ 0.0° (c 3.76, chloroform). Undecarboxylated (−)-I recovered from the aqueous phase displayed $[\alpha]^{25}_{546}$ −80.7° (c 3.5, 95% ethanol), weight 0.144 g. The optical stability of the product, 2-methyl-2,3-dihydrobenzothiophene 1-dioxide (II), was not tested under the conditions of run 19. Such a control run was made for run 15 (t-butyl alcohol as solvent) since the possibility existed that a very small equilibrium concentration of t-butoxide anion was formed which rapidly racemized the product. In dimethyl sulfoxide, however, in the presence of excess acid throughout the time of reaction (55% decarboxylation with 8 mole % base), the existence of a strongly basic species seemed remote.

Run 20 was conducted similarly to the experiment described below for the preparation of (−)-II-*d*. Run 21 was conducted similarly to the experiment described below for the preparation of (+)-II-*h*.

In general, if recovery of undecarboxylated (−)-I was desired, the aqueous solution of its ammonium or potassium salt was acidified with excess sulfuric acid after isolation of the product, (+)-II. Recovery of the acid was effected by two or three extractions of the acidic aqueous solution with an equal volume of chloroform per extraction. Evaporation of chloroform after drying yielded crystalline (−)-I. Determination of the optical purity of recovered acid was always done without any purification of the substance because of its marked tendency to fractionate. Thus, the possibility

of error in determining the true optical impurity of recovered (−)-I was reduced.

Two additional decarboxylation experiments (not reported in Table II) were conducted in the absence of solvent. In the first, 250 mg of pyridine salt of optically pure (−)-I was heated at 180° for 44 min to produce 120 mg of II (isolated by above procedures), $[\alpha]^{25}_{546}$ +4.1° (c 4.6, chloroform). In a second experiment, 30.5 mg of the same pyridine salt was mixed with 226 mg of optically pure (−)-I, and the melt was heated for 2 hr (∼0.5 mm). A white substance sublimed out of the melt. Both starting material [105 mg, $[\alpha]^{25}_{546}$ −78.5° (c 2.9, 95% ethanol)] and II (18 mg) were isolated by the above procedures, $[\alpha]^{25}_{546}$ 0.00° (c 4.6, chloroform).

Stability of (−)-2-Methyl-2,3-dihydrobenzothiophene-2-carboxylic Acid 1-Dioxide in the Absence of Base. A solution of 0.300 g of (−)-I,$[\alpha]^{25}_{546}$ −83.9°(c 3.3, 95% ethanol), in 10 ml of t-butyl alcohol was heated for 24 hr at 164°, and the product was put through the same isolation procedure as in run 15. The benzene extracts contained no II. The aqueous phase was acidified with sulfuric acid and extracted with two 30-ml portions of chloroform. The chloroform layer was washed with water, dried, and evaporated under reduced pressure. The recovered acid, 0.277 g (92%), displayed $[\alpha]^{25}_{546}$ −81.5° (c 3.4, 95% ethanol). Similar results were obtained in water (48 hr at 164°) and dimethyl sulfoxide (1.3 hr at 142°).

Optical Stability of (+)-2-Methyl-2,3-dihydrobenzothiophene 1-Dioxide ((+)-II) under Conditions of Its Formation (Control for Run 15). A 0.200-g portion of (+)-II, $[\alpha]^{25}_{546}$ +14.0° (c 3.9, chloroform), 0.267 g of optically pure (−)-I, and 0.0324 g of ammonium salt of (−)-I, $[\alpha]^{25}_{546}$ −61.0° (c 2.9, water) were placed in an ampoule with 10 ml of t-butyl alcohol, and the ampoule was sealed under nitrogen. The ampoule was thermostated at 164° for 7 hr, cooled, and opened, and the decarboxylation reaction mixture was worked up identically with that of run 15. The product, (+)-II, 0.238 g, displayed $[\alpha]^{26}_{546}$ +11.2°. Acidification of the aqueous phase followed by extraction with chloroform provided 0.220 g of (−)-I, $[\alpha]^{25}_{546}$ −80.6° (c 3.6, 95% ethanol). A calculaton was made of the specific rotation that the product should have had in this experiment if the decarboxylation reaction were zero order in ammonium salt until 90% reaction and if the product of the decarboxylation reaction were optically inactive. In run 15, 35% reaction occurred in 14 hr; therefore, 17% reaction should occur in 7 hr, yielding 0.042 g of product. The total amount of sulfone present should thus have been 0.242 g, $[\alpha]^{25}_{546}$ 0.827 × +14.0° or +11.6°, and 0.241 g of acid should have remained undecarboxylated.

Preparation of (+)-2-Methyl-2,3-dihydrobenzothiophene 1-Dioxide ((+)-II). A solution of 32.3 g of the ammonium salt of (−)-I, $[\alpha]^{25}_{546}$ −61.0° (c 3.1, water), was dissolved in 242 ml of distilled water. To this solution was added 8.5 g of glacial acetic acid. The mixture was transferred into a number of 140-ml capacity, heavy-walled glass ampoules, previously purged with nitrogen, in 37.5-ml portions, and the ampoules were sealed. Each was heated to 155° for 48 hr. The ampoules were cooled and opened, and 70 ml of benzene was added to each. After thorough shaking, the layers were separated, and the combined aqueous phase was extracted with an additional 350 ml of benzene. The benzene solution of the product was washed with 150 ml of 10% aqueous sodium carbonate solution and 200 ml of water, dried, and evaporated, yielding 22.85 g of (+)-II, $[\alpha]^{26}_{546}$ +13.23° (c 4.0, chloroform) (94.2% as a light yellow solid). The sulfone, 22.8 g, prepared above was fractionally crystallized beginning with 1450 ml of boiling ether as follows: crop 1, 6.15 g,$[\alpha]^{25}_{546}$ +2.3° (c 4.1, chloroform); crop 2, 1.1 g (from 1080 ml of ether), +3.18°; crop 3, 2.40 g (from 880 ml of ether), +3.68°; crop 4, 1.65 g (from 525 ml of ether), +6.94°; crop 5, 0.76 g (from 400 ml of ether), +8.68°; crop 6, 0.58 g (from 235 ml of ether), +11.68°; crop 7, 3.47 g (from 130 ml of ether), +23.75°; crop 8, 2.58 g (from 80 ml of ether), +23.93°; crop 9, 1.44 g (from 55 ml of ether), +23.80°; crop 10, 1.12 g (from 30 ml of ether), +24.00°; crop 11, 0.78 g (from 15 ml of ether), +24.20°; crop 12, 0.28 g (from 9 ml of ether), +24.10°; crop 13, 0.28 g (from 3 ml of ether), +24.08°. All rotations were taken in chloroform at 546 mμ in a 1-dm polarimeter tube with c 4.0 ± 0.15. The average rotation of the last six fractions was +24.02°. The melting point of racemic 2-methyl-2,3-dihydrobenzothiophene 1-dioxide was 115.5–116.5°, while that of material displaying $[\alpha]^{25}_{546}$ +24.1° was 74–75°. Material with rotation between 0 and +24.1° did not melt sharply. Mixtures of racemic and active II gave material which melted below either single component. *Anal.* Calcd for $C_9H_{10}SO_2$: C, 59.34; H, 5.49; S, 17.60. Found: C, 59.52; H, 5.44; S, 17.75.

Isotopic Exchange of (+)-2-Methyl-2,3-dihydrobenzothiophene-2-carboxylic Acid 1-Dioxide. The acid, 46.7 g, $[\alpha]^{26}_{546}$ +82.0° (c 3.3, ethanol), was added to a mixture of 110 g of deuterium oxide (99.77 atom % deuterium) and 100 ml of tetrahydrofuran (freshly distilled from calcium hydride). The mixture was refluxed for 24 hr and cooled, and the tetrahydrofuran was removed under reduced pressure. The exchanged acid was recovered by three extractions of the deuterium oxide with 200-ml portions of chloroform. Evaporation of the chloroform yielded 46.5 g of the deuterated acid.

Ammonium Salt N-d_4 of (+)-2-Methyl-2,3-dihydrobenzothiophene-2-carboxylic Acid-O-d 1-Dioxide. The exchanged acid as prepared above, 10.0 g, was dissolved in 625 ml of ethyl ether. Into the rapidly stirred solution was bubbled ammonia-d_3 gas generated by the controlled hydrolysis of 16.0 g of magnesium nitride with 25 ml of deuterium oxide.[19] A slow stream of purified, dry nitrogen gas was kept flowing through the apparatus at all times. A 2 × 60 cm column of potassium hydroxide served to dry the ammonia-d_3 before reaction with the acid. Precipitation of the salt was quantitative after 40 min. The ammonium salt N-d_4, 10.8 g (99%), was obtained as a white solid, $[\alpha]^{25}_{546}$ +59.4° (c 3.0, deuterium oxide).

(−)-2-Deuterio-2-methyl-2,3-dihydrobenzothiophene 1-Dioxide ((−)-2-d-II). A solution of 2.0 g of the above ammonium salt in 13.5 ml of deuterium oxide prepared. To the solution was added 1.67 ml of 5.80 M acetic acid-O-d in deuterium oxide (prepared by hydrolysis of freshly distilled acetic anhydride in deuterium oxide under nitrogen at 60° with a trace of sulfuric acid added). The mixture was transferred to a 60-ml, heavy-walled glass ampoule; the ampoule was sealed under nitrogen and placed in a constant-temperature bath at 155° for 48 hr. The ampoule was cooled and opened. A 40-ml aliquot of benzene was added, and the product was isolated as described above, 1.48 g (98% as colorless solid), $[\alpha]^{25}_{546}$ −11.0° (c 3.9, chloroform). The deuteriosulfone, 34.33 g, prepared as described above, was fractionally crystallized as in the preparation of nondeuterated material. The rotations of crops 9–13 ranged from $[\alpha]^{25}_{546}$ −24.08 to −24.18° (c 4, chloroform). These were combined and crystallized again, 11.2 g, mp 73–74°, $[\alpha]^{25}_{546}$ −24.1° (c 4, chloroform).

Combustion and deuterium analysis by the falling drop method gave 97.7% of 1 g atom of deuterium. *Anal.* Calcd for C_9H_9DSO_2$: C, 58.99; H_2O + D_2O, 0.497 mg/mg of sample; S, 17.50. Found: C, 59.09; H_2O + D_2O, 0.477 mg/mg of sample; S, 17.50. Racemic II-d was obtained by fractional crystallization of the filtrates, 16 g, mp 115–116°.

Maximum Rotation of (+)-2-Methyl-2,3-dihydrobenzothiophene 1-Dioxide ((+)-II) by Isotopic Dilution Analysis. A 0.716-g portion of 99 ± 1% racemic II-d, 0.984–0.986 atom of deuterium per molecule,[6b] and 0.478 g of (+)-II, $[\alpha]^{25}_{546}$ +23.8° (c 3.9, chloroform) (deuterio racemate–protio antipode 60:40) were dissolved in 85 ml of boiling ether. Upon cooling, a crop of crystals separated, 0.368 g. This material was recrystallized from 32 ml of the same solvent, 0.102 g, $[\alpha]^{25}_{546}$ +0.28° (c 4.0, chloroform). The recrystallized, sublimed sulfone was found to contain 0.701 atom of deuterium per molecule.[6b] Continued fractional crystallization of the mother liquor from crop 1 yielded crop 7, 0.183 g, $[\alpha]^{25}_{546}$ +23.8° (c 4.5, chloroform). The sublimed recovered (+)-antipode was found to contain 0.427 atom of deuterium per molecule.[6b] Based on the molecular formula $C_9H_{10}SO_2$, the recovered racemate was 70.1% deuterated, while the recovered antipode was 42.7% deuterated. These data were used to calculate the optical purity of (+)-II using material with a specific rotation of +23.8°. The maximum rotation of (±)-II turned out to be $[\alpha]^{25}_{546}$ ±24.04 ± 0.4°.

Solvents, Bases, and Gases. The solvent, t-butyl alcohol, was dried over molecular sieves (Linde, Type 4A, pellets) for several days and distilled. The middle fraction was stored over molecular sieves. The basic solutions of t-butyl alcohol were prepared by reaction of a weighed amount of clean potassium metal with the solvent in a dry purified nitrogen atmosphere. Ethylene glycol was similarly purified and stored. The basic solution was prepared by adding clean potassium metal to the purified solvent in a dry purified nitrogen atmosphere at ice–salt bath temperature. Ethylene glycol-O-d_2 was available from a previous investigation[3c] (1.97 atoms of deuterium per molecule). Dimethyl sulfoxide was prepared and stored in the same way. The basic solution of dimethyl sulfoxide–methanol was prepared by adding clean potassium metal to pure methanol in a dry purified nitrogen atmosphere and

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(19) R. H. Herber, "Inorganic Isotope Synthesis," W. A. Benjamin, Ine., New York, N. Y., 1962, p 36.

adding the resulting solution to dimethyl sulfoxide. Methanol ("Baker Analyzed" reagent) was refluxed over and distilled from calcium hydride and then stored over molecular sieves. Methanol-O-d (0.986 atom of deuterium per molecule) was available from another investigation.[20]

Final base concentrations were determined by titration in aqueous solution with standard acid. Nitrogen was purified by first passing through a tube containing calcium sulfate and ascarite, then through two 2 × 20 cm tubes containing copper turnings heated to 300°, and finally through another tube containing calcium sulfate and ascarite.

Typical Exchange and Racemization of (−)-2-Deuterio-2-methyl-2,3-dihydrobenzothiophene 1-Dioxide ((−)-II-d) (Run 2). A 0.1809-g portion of (−)-II-d, $[\alpha]^{25}_{546}$ −24.1° (c 3.95, chloroform), was weighed into a 3-ml volumetric flask, and the flask was filled to the mark with a solution of 0.028 N potassium t-butoxide in t-butyl alcohol-tetrahydrofuran 70:30 (0.331 M substrate). The flask was thoroughly shaken and thermostated at 25° within 90 sec from initial contact between the base-solvent and substrate. After 1.05 hr, the contents of the volumetric flask were poured into a 125-ml separatory funnel (Teflon greaseless stopcock) containing 40 ml of water to which 0.50 ml of concentrated hydrochloric acid and 35 ml of benzene had been added. The funnel was vigorously shaken; the layers were separated, and the aqueous phase was extracted with two additional 30-ml portions of benzene. The combined benzene extracts were washed three times with 30-ml portions of water, dried, and evaporated under reduced pressure. The product, 0.179 g, was totally sublimed [80° (0.15 mm)] and examined for optical purity and deuterium content. The substance displayed $[\alpha]^{25}_{546}$ −10.40° (c 4.02, chloroform) and was found by the combustion and falling drop method to contain 0.56 atom of deuterium per molecule. This corresponds to 56.8% racemization and 48.3% loss of deuterium (corrected for 0.977 atom of deuterium before exchange).

General Procedure for Racemization and Exchange of (−)-2-Deuterio-2-methyl-2,3-dihydrobenzothiophene 1-Dioxide ((−)-II-d). Run 1 was conducted identically with that of run 2, except the solvent was dimethyl sulfoxide–MeOH 91:9 (by volume; 2.3 M in CH₃OH), 0.16 M in MeOK. Runs 3 and 4 involved ampoule techniques and were conducted as follows. A 0.180-g portion of (−)-II-d was weighed into a 6-ml volumetric flask, and the flask was filled to the mark with either 0.16 N potassium methoxide (0.96 mmole) in methanol or 0.16 N potassium methoxide in methanol-O-d (0.164 M substrate). The volumetric flask was thoroughly shaken, and its contents were transferred to a nitrogen-purged ampoule with the aid of a syringe. The ampoule was sealed and placed in a constant-temperature bath at 76.0° for 11.5 hr (run 3) or 9.75 hr (run 4). The product was isolated and analyzed as described above, except that the aqueous phase of the run 3 work-up was titrated with standard acid for base. No loss of base occurred during reaction within experimental error (18.7 ml of 0.0513 M HCl required for phenolphthalein end point, 0.95 mmole). Run 5 was also conducted in an ampoule. Since the sulfone was insoluble in ethylene glycol, a 0.216-g portion was weighed directly into an ampoule, 20.0 ml of ethylene glycol 0.059 N in potassium ethylene glycoside (1.18 mmoles of base) was added from a pipet, and the ampoule was purged and sealed; the sulfone dissolved when heated (0.06 M in substrate). Isolation and analysis of the product was conducted similarly to run 3. (Titration of the aqueous phase of the work-up required 22.9 ml of 0.0513 N HCl, 1.17 mmoles.) Run 6 was conducted similarly to run 5, except that 0.125 g of sulfone was used. The base-solvent was 0.10 N potassium ethylene glycoxide-O-d in ethylene glycol-O-d₂.

Large-Scale Racemization and Exchange Experiment on (−)-2-Deuterio-2-methyl-2,3-dihydrobenzothiophene 1-Dioxide ((−)-II-d). Into a 20-ml volumetric flask was weighed 1.215 g of (−)-II-d, $[\alpha]^{25}_{546}$ −24.08° (c 4.0, chloroform). The flask was filled to the mark with the same solvent as used in run 2 (see above), shaken thoroughly, and thermostated at 25.0° for 675 min. The isolated product, 1.194 g of exchanged sulfone, displayed $[\alpha]^{25}_{546}$ −9.68° (c 4.0, chloroform), or 59.8% racemized.

This material was fractionally crystallized from ether as follows: crop 1, 0.231 g (from 85 ml), $[\alpha]^{25}_{546}$ −1.49° (c 4.0, chloroform). Crop 1 was then recrystallized from 20 ml of ether and crop 1-A separated, 0.127 g, $[\alpha]^{25}_{546}$ −0.2° (c 4.0, chloroform). The racemic modification of the exchange product was found to be 60.5% exchanged.[6a] The mother liquor remaining after crop 1 separated

was concentrated to 60 ml and crop 2 separated, 0.334 g. Continued fractional crystallization of the exchanged sulfone yielded the following: crop 3, 0.083 g (from 35 ml); crop 4, 0.083 g (from 20 ml); crop 5, 0.042 g (from 10 ml); crop 6, 0.107 g (from 5 ml) (crystal form change); crop 7, 0.117 g (from 2 ml), $[\alpha]^{25}_{546}$ −23.7° (c 4.0, chloroform). Evaporation of the mother liquor from crop 7 yielded 0.144 g of exchanged sulfone after chromatography, $[\alpha]^{25}_{546}$ −23.5° (c 4.0, chloroform). Crop 7, mp 72.5–73°, was totally sublimed [85° (0.15 mm)] and analyzed for deuterium,[6a] 70.0 atoms % (excess) deuterium, or 28.3% exchanged (corrected for 0.977 atom of deuterium per molecule before exchange). These data were used to determine the relative rates of retention, inversion, and isoinversion, and to reduce k_e/k_α for racemization vs. exchange to time zero.

Racemization of (+)-2-Methyl-2,3-dihydrobenzothiophene 1-Dioxide and (−)-2-Deuterio-2-methyl-2,3-dihydrobenzothiophene 1-Dioxide in t-Butyl Alcohol. Two racemization runs were conducted at 25.0° with identical concentrations of substrate in the same base-solvent system used in run 2 (see above): 0.1215 g of either (+)-II, $[\alpha]^{25}_{546}$ +24.05° (c 4.0, chloroform), or (−)-II-d, $[\alpha]^{25}_{546}$ −24.10° (c 4.0, chloroform), was weighed into a 2-ml volumetric flask. The flask was filled to the mark with thermostated base-solvent and vigorously shaken. The thermostated polarimeter tube was immediately filled and rotations were taken on a Perkin-Elmer Model 141 polarimeter, the first reading at time 3 min. Thirteen points were taken during the first 75% of the reaction. The logarithm of the rotation was plotted against time, and the slope of the straight line was determined graphically to be 2.90 ± 0.003 × 10⁻⁴ sec⁻¹ (protiosulfone) and 2.24 ± 0.016 × 10⁻⁴ sec⁻¹ (deuteriosulfone) (deviations calculated by least-squares method). These data were used to reduce racemization and exchange kinetics of (−)-II-d in t-butyl alcohol to time zero. Table IV records the kinetic data for racemization of (−)-II-d.

The products from the isotopic dilution experiment, those from the reresolution experiment, and a series of standards were analyzed for deuterium on an Associated Electronics Industries MS 9 mass spectrometer by comparison of the relative intensities of the mass 182 and 183 peaks (parent peaks of II-h and II-d). The deuterium contents found for the standards were within ±0.5% of the theoretical values.

2-Carbethoxytetrahydrothiophene. The substance, tetrahydrothiophene-2-carboxylic acid[21b] (100 g, mp 51°), was esterified with 800 ml of ethyl alcohol and four drops of hydrochloric acid. The reaction mixture was refluxed for 72 hr; excess ethanol was removed by evaporation under reduced pressure leaving a light yellow oil which was distilled. A fraction, bp 102.5–104° (11 mm), 101.2 g (92.5%), was retained. *Anal.* Calcd for C₇H₁₂SO₂: C, 52.52; H, 7.50. Found: C, 52.51; H, 7.59.

Table IV. Racemization of a 0.33 M Solution of (−)-2-Deuterio-2-methyl-2,3-dihydrobenzothiophene 1-Dioxide ((−)-II-d)[a] at 25.0° Followed to >85% Reaction

α_{obsd}, deg	Time, min	α_{obsd}, deg	Time, min
−1.380	3	−0.548	70
−1.253	10	−0.479	80
−1.091	20	−0.419	90
−0.948	30	−0.367	100
−0.825	40	−0.345	105
−0.718	50	−0.209	145
−0.627	60		

$$k^D_{\alpha_{obsd}} = 2.24 \pm 0.016 \times 10^{-4} \text{ sec}^{-1}$$

[a] 0.98 atom of deuterium per molecule. In t-butyl alcohol-tetrahydrofuran (70:30) (0.028 M in potassium t-butoxide).

2-Carbethoxytetrahydrothiophene 1-Dioxide. To a solution of 25 g of the above ester in 75 ml of glacial acetic acid in a 250-ml flask was added 48 ml of 30% hydrogen peroxide in 2-ml portions with vigorous swirling. Ice-bath cooling, both during and after addition of hydrogen peroxide was complete, was employed *whenever* the temperature of the reaction mixture exceeded 39° until cooling to 35° was achieved. After the exothermic reaction

(20) D. J. Cram and A. S. Wingrove, *J. Am. Chem. Soc.*, **86**, 5490 (1964).

(21) (a) E. V. Whitehead, R. A. Dean, and F. A. Fidler, *J. Am. Chem. Soc.*, **73**, 3634 (1951); (b) F. Ernst, *Ber.*, **20**, 518 (1887).

subsided, the reaction mixture was allowed to stand at 25° for 20 hr. It was then shaken with 200 ml of dichloromethane. The layers were separated, and the aqueous phase was extracted twice more with 200-ml portions of dichloromethane. The combined dichloromethane extracts were cooled to 0° and washed once with 150 ml of ice water, once with 50 ml of cold saturated ferrous sulfate solution, and once with 100 ml of cold saturated sodium bicarbonate solution. Evaporation of dichloromethane after drying yielded an oil which was distilled; the product was collected at bp 117–119° (0.35 mm), 18.2 g (59% as colorless oil). *Anal.* Calcd for $C_7H_{12}SO_4$: C, 43.76; H, 6.25; S, 16.69. Found: C, 43.62; H, 6.44; S, 16.29.

2-Methyl-2-carbethoxytetrahydrothiophene 1,1-Dioxide. A solution of 14.0 g of sodium metal in 300 ml of absolute ethanol was prepared. To the stirred solution, cautiously maintained at 70°, was added dropwise a solution of 73 g of 2-carbethoxytetrahydrothiophene 1-dioxide in 150 ml of absolute ethyl alcohol. The reaction mixture was stirred at 70° for 2 hr and cooled to 40°, and 90 g of methyl iodide was added dropwise. The reaction mixture was then heated very slowly to 70° for an additional 18 hr. The contents of the flask were then shaken with 200 ml of water and 300 ml of ether. The aqueous phase was extracted with two additional 200-ml portions of ether; the ether extracts were combined, cooled once with 100 ml of ice water, and dried. Evaporation of the ether left an oil which was distilled, the product being collected at bp 107–108° (0.35 mm), 69.0 g (88% as light yellow oil). *Anal.* Calcd for $C_8H_{14}SO_4$: C, 46.78; H, 6.72; S, 15.55. Found: C, 46.60; H, 6.84; S, 15.36.

2-Methyltetrahydrothiophene-2-carboxylic Acid 1-Dioxide (III). Into a stirred solution of 15 g of sodium hydroxide in 210 ml of water, 69 g of the above ester was poured in a thin stream. Stirring was continued for 15 min, 40 ml of 96% sulfuric acid was added slowly with ice-bath cooling, and the acidified hydrolysis reaction mixture was saturated with sodium chloride. Continuous extraction with chloroform for 48 hr yielded 59.1 g (92.5%) of III, mp 158–159.5°. *Anal.* Calcd for $C_6H_{10}SO_4$: C, 40.46; H, 5.61; S, 17.96. Found: C, 40.57; H, 5.72; S, 17.80.

(+)-2-Methyltetrahydrothiophene-2-carboxylic Acid 1,1-Dioxide ((+)-III). A solution of 75.3 g of III and 169.3 g of brucine in 1600 ml of hot water was prepared. The solution was allowed to cool very slowly to 7°, and the salt (111.2 g) separated as large plates. Recrystallization of the salt from hot water yielded 93.0 g (38%) of material. A small portion of the salt was converted to the free acid which, after sublimation, exhibited $[\alpha]^{26}_{546} +20.4°$. Additional crystallizations of the salt provided no change in rotation of the derived acid. The optically pure salt (88 g, 36%) was dissolved in 800 ml of warm water, and a solution of 21 g of potassium carbonate in 50 ml of water was added with rapid stirring. Precipitation of brucine was complete within 15 min. The slurry was filtered; the filtrate was extracted twice with 300-ml portions of chloroform and reduced in volume to 225 ml under vacuum. Sulfuric acid, 45 ml, was added with cooling, and the acidic solution was saturated with sodium chloride. Continuous extraction of the solution with chloroform yielded 22.8 g of crude (+)-III. Recrystallization of the acid from 50 ml of ether gave 16.6 g of (+)-III, mp 161.5–162.5°, $[\alpha]^{28}_{546} +20.4°$ (c 4.7, water).

(−)-2-Methyltetrahydrothiophene-2-carboxylic Acid 1,1-Dioxide ((−)-III). To the mother liquors from the first crystallization of the brucine salt of III was added a solution of 25 g of potassium carbonate in 50 ml of water with rapid stirring, and the acid was recovered as before. The crude, partially optically active acid was placed in 55 ml of ether and warmed; the warm solution was filtered. The residue from filtration was found to be racemic, $[\alpha]^{28}_{546} 0.0°$ (c 4.7, water). Cooling of the filtrate afforded 14.04 g of (−)-III, mp 159–160°, $[\alpha]^{28}_{546} −20.2°$ (c 4.7, water).

Ammonium Salt of (+)-2-Methyltetrahydrothiophene-2-carboxylic Acid 1-Dioxide. Anhydrous ammonia gas was bubbled into a solution of 1 g of (+)-III, $[\alpha]^{29}_{546} +20.4°$, in 30 ml of ether for 30 min. The salt, 1.058 g (98%), was collected by filtration, washed four times with 25 ml of ethyl ether, and vacuum dried, $[\alpha]^{27}_{546} +13.95°$ (c 4.3, water), mp 170° dec.

Representative Decarboxylation of (+)-2-Methyltetrahydrothiophene-2-carboxylic Acid 1-Dioxide ((+)-III) (Run 23). Into a dry ampoule, thoroughly purged with purified nitrogen gas, was introduced a solution of 0.137 g of optically pure ammonium salt of (+)-III, $[\alpha]^{27}_{546} +13.95°$ (c 4.3, water), and 0.363 g of optically pure (+)-III, $[\alpha]^{28}_{546} +20.4°$ (c 4.7, water), in 10 ml of distilled water. The ampoule was sealed and placed in a constant-temperature bath at 165°. After 236 hr, the ampoule was opened, and the contents were removed. Evaporation of water under reduced

pressure left a semisolid which was taken up in 30 ml of ether. Dry ammonia gas was bubbled into the solution for 30 min and ammonium salt of (+)-III separated. The solid ammonium salt was recovered by filtration and dried under vacuum, 0.355 g, $[\alpha]^{26}_{546} +13.9°$ (c 4.2, water). The weight of recovered ammonium salt corresponded to 0.199 g of free acid remaining in the decarboxylation reaction mixture after 236 hr. Thus, decarboxylation proceeded to 45% of completion. Evaporation of the filtrate left an oil which was chromatographed on 40 g of silica gel in an 18-mm diameter column with ether–pentane, 75:25, as developer. Optically active IV was obtained analytically pure, 0.075 g, $[\alpha]^{27}_{546} +5.60°$ (c 7.0, 95% ethanol). The infrared and nmr spectra of this substance were identical with those of an authentic sample of 2-methyltetrahydrothiophene 1-dioxide (see above).

Run 22 was similarly conducted, except that 0.0435 g of anhydrous potassium carbonate was used as base with 0.450 g of (+)-III in 10 ml of distilled water. Decarboxylation proceeded to 53.6% of completion as determined by recovery of undecarboxylated acid as its ammonium salt. The weight of potassium carbonate used was subtracted from the total weight of recovered solids in determining per cent decarboxylation. Run 24 was conducted identically with that of run 22, and run 25 was conducted identically with that of run 23.

Optical Stability of (+)-2-Methyltetrahydrothiophene 1-Dioxide ((+)-IV) under Conditions of Its Formation (Control for Run 24). Sulfone (+)-IV, 0.155 g, $[\alpha]^{26}_{546} +5.41°$ (c 9.7, ethanol), 0.450 g of (+)-III, $[\alpha]^{27}_{546} +20.4°$ (c 4.7, water), 0.0435 g of anhydrous potassium carbonate, and 10 ml of *t*-butyl alcohol were placed in an ampoule. The ampoule was purged with dry nitrogen gas, sealed, and placed in a constant-temperature bath at 165° for 3 hr. The product, after isolation in the above manner and purification by chromatography on silica gel, exhibited $[\alpha]^{26}_{546} +4.07°$ (c 9.8, ethanol), 0.188 g (theory requires $[\alpha]^{26}_{546} +4.0°$). The infrared and nmr spectra of (+)-IV recovered in this experiment were identical with those of (+)-IV obtained from other runs and with those taken of IV synthesized by a known procedure.[20a]

Stability of (+)-2-Methyltetrahydrothiophene-2-carboxylic Acid 1-Dioxide in the Absence of Base. A solution of 0.450 g of (+)-III in 10 ml of *t*-butyl alcohol was heated to 165° for 24 hr, and the product was put through the same isolation procedure as in run 23. Ammonium salt of (+)-III, 0.470 g (95%), $[\alpha]^{26}_{546} +13.8°$ (c 4.2, water) was the only product isolated. Similar results were obtained in water.

5-Methyl-2-carbethoxytetrahydrothiophene. An amalgam was prepared from 69 g of sodium metal and 3500 g of mercury and was added while still molten to a stirred solution of 53 g of 5-methylthiophene-2-carboxylic acid (Marstan Chemical Laboratory) and 16 g of sodium hydroxide in 550 ml of water. After the initial vigorous reaction had subsided, the reaction mixture was heated to 85° and stirred at this temperature for 6 days. The spent amalgam was separated from the aqueous phase, and the latter was acidified with 350 ml of concentrated hydrochloric acid at 0° with rapid stirring. The heavy oil that separated was recovered by extraction with four 250-ml portions of ether. The combined ether extracts were washed twice with 250-ml portions of saturated sodium chloride solution, dried, and evaporated, yielding 48.2 g of crude acid which was esterified directly with 500 ml of absolute ethyl alcohol and four drops of hydrochloric acid. Evaporation of excess ethanol yielded an oil which was distilled, bp 103–105° (12 mm), 44 g (67.5% over-all as colorless oil). *Anal.* Calcd for $C_8H_{14}SO_2$: C, 55.17; H, 8.04; S, 18.41. Found: C, 55.41; H, 8.00; S, 18.18.

5-Methyl-2-carbethoxytetrahydrothiophene 1-Dioxide. To a solution of 30.8 g of 5-methyl-2-carbethoxytetrahydrothiophene in 85 ml of glacial acetic acid in a 250-ml flask was added 54 ml of 30% hydrogen peroxide in 5-ml portions with vigorous swirling. Ice-bath cooling, both during and after addition of hydrogen peroxide was complete, was employed *whenever* the temperature of the reaction mixture exceeded 40°. After the exothermic reaction subsided, the reaction mixture was allowed to stand at 25° for 30 hr and shaken with 200 ml of dichloromethane. The layers were separated, and the aqueous phase was extracted twice more with 200-ml portions of dichloromethane. The combined dichloromethane extracts were cooled to 0° and washed once with 150 ml of ice water, once with 50 ml of cold saturated ferrous sulfate solution, and once with 100 ml of cold saturated sodium bicarbonate solution, in that order. Evaporation of dichloromethane left an oil which was distilled, the product being collected at bp 114–117° (0.25 mm), 20.2 g (55.4% as colorless oil). *Anal.* Calcd for $C_8H_{14}SO_4$: C, 46.61; H, 6.79; S, 15.55. Found: C, 46.78; H, 6.78; S, 15.39.

5-Methyltetrahydrothiophene-2-carboxylic Acid 1-Dioxide (V). Into a stirred solution of 25 g of sodium hydroxide in 210 ml of water was poured 80.7 g of the above ester in a thin stream. Stirring was continued for 45 min; 60 ml of 96% sulfuric acid was added slowly with ice-bath cooling, and the acidic solution was saturated with sodium chloride. Continuous extraction of the solution with chloroform for 48 hr yielded after evaporation of solvent 68 g (99%) of V as a semisolid.

Racemate A of 5-Methyltetrahydrothiophene-2-carboxylic Acid 1-Dioxide (V). The mixture of racemates obtained above was dissolved in 300 ml of boiling chloroform, and hexane was added until the solution was nearly saturated at the boiling point of the mixture. The solution was allowed to cool open to the atmosphere, and a crop of white crystals separated which was recrystallized twice from chloroform, 26 g, mp 121–124°. The nmr spectrum of the recrystallized acid (V-A) contained only one doublet for the methyl group (τ 8.80, $J = 6.5$ cps), whereas the spectrum of the crude mixture of racemates contained a closely spaced double doublet (τ 8.80, $J = 6.5$ cps and τ 8.63, $J = 6.0$ cps). Attempts to resolve this material through its brucine salt were only partially successful.

(+)-5-Methyltetrahydrothiophene-2-carboxylic Acid 1-Dioxide of Racemate B ((+)-V-B). A solution of 42.7 g of V (composition: about 14.9 g of racemate A and 32.3 g of racemate B, nmr analysis) and 104 g of brucine in 236 ml of hot water was prepared. After standing at 25° for 12 days, a crystalline salt began to separate; an additional two weeks was required before separation of the salt ceased, 39.7 g (26.2%). The derived acid recovered after an additional crystallization of the salt from water displayed $[\alpha]^{26}_{546}$ +34.2° (c 5.1, chloroform). A third crystallization of the salt gave recovered acid of $[\alpha]^{28}_{546}$ +34.9° (c 4.9, chloroform); a fourth crystallization of the salt yielded acid of $[\alpha]^{26}_{546}$ +34.4° (c 4.9, chloroform). The salt thrice crystallized as above, 7.35 g, was dissolved in 100 ml of warm water and a solution of 7 g of potassium carbonate in 15 ml of water was added. Precipitation of brucine was complete within 15 min. The slurry was filtered, reduced in volume to 25 ml under vacuum, and filtered. The solution of the potassium salt of (+)-V-B was acidified with sulfuric acid and continuously extracted with chloroform for 48 hr. Recovered (+)-V-B, 1.356 g, $[\alpha]^{28}_{546}$ +34.9° (c 4.9, chloroform), mp 79–81°, was recrystallized from ether–pentane, 1.21 g, $[\alpha]^{26}_{546}$ +35.1° (c 4.9, chloroform), mp 79.5–81°. An additional crystallization of the substance did not change these properties. *Anal.* Calcd for C_6H_{10}-SO_4: C, 40.46; H, 5.61; S, 17.96. Found: C, 40.53; H, 5.68; S, 17.67.

Decarboxylation of (+)-5-Methyltetrahydrothiophene-2-carboxylic Acid 1-Dioxide ((+)-V-B). A solution of 0.388 g of optically pure (+)-V-B, $[\alpha]^{26}_{546}$ +35.1° (c 4.9, chloroform), and 0.137 g of the ammonium salt of optically pure (+)-V-B, $[\alpha]^{26}_{546}$ +23.61° (c 0.66, water), was prepared in 10 ml of water. The solution was placed in an ampoule which had been thoroughly purged with nitrogen. The ampoule was sealed and placed in a constant-temperature bath at 164° for 72 hr. After this time, the ampoule was opened, and its contents were removed. Water was evaporated under reduced pressure, leaving a viscous oil which was taken up in 20 ml of methanol–ether. Ammonia gas was bubbled into the solution for 30 min to convert excess acid to the ammonium salt. The solvent was removed under reduced pressure, and the residue was extracted with two 30-ml portions of boiling ether. The solid ammonium salt remaining after extraction exhibited $[\alpha]^{26}_{646}$ +23.40° (c 0.64, water), 0.324 g. Decarboxylation thus proceeded to 43% of completion. Since only 25 mole % ammonium salt was employed as base, the decarboxylation reaction mixture was always acidic. Thus, the product could not have been partially racemized.

The ether extracts were evaporated yielding an oil which was chromatographed on a 1 × 30 cm column of silica gel with ethyl ether–pentane, 70:30, as eluent. The sulfone, optically pure (+)-IV, purified by chromatography, 0.120 g, exhibited $[\alpha]^{25}_{546}$ +11.80° (c 3.5, ethanol). The infrared and nmr spectra of this substance were identical with those of (+)-IV obtained by decarboxylation of 2-methyltetrahydrothiophene-2-carboxylic acid 1-dioxide and to those of racemic IV obtained *via* an independent synthesis reported above.[21a]

Electrophilic Substitution at Saturated Carbon. XXXIV. Isoinversion as a Mechanistic Component in Base-Catalyzed Hydrogen–Deuterium Exchange between Carbon Acids and Medium[1]

Warren T. Ford,[2] Edward W. Graham, and Donald J. Cram

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Abstract: Analysis of the over-all stereochemical course of base-catalyzed hydrogen–deuterium exchange reactions of carbon acids in terms of mechanistic components is provided by a kinetic model. Rate constants for exchange with retention of configuration, exchange with inversion, and isoinversion (defined as inversion without exchange) have been determined for exchange of I-H+ in methanol-O-d with potassium methoxide at 25° by two experimentally independent methods based on the model. One method used only kinetics, and the other used reresolution of partially racemized material. Exchange of I-D+ in t-butyl alcohol with potassium phenoxide was also investigated by the latter method. Isoinversion is shown to be a contributing mechanistic component in both media. Primary substrate and solvent isotope effects on racemization of I are reported. The results are interpreted by a mechanism in which carbanions are tightly hydrogen bonded to just one solvent molecule at a time.

The stereochemical courses of hydrogen–deuterium exchange reactions of carbon acids have been divided into four categories on the basis of their k_e/k_α

(rate constant for exchange over that for racemization) values: exchange with net retention ($k_e/k_\alpha > 1.0$), exchange with total racemization ($k_e/k_\alpha = 1.0$), exchange with net inversion ($0.5 \leq k_e/k_\alpha < 1.0$), and isoracemization (defined as racemization without exchange,

$k_e/k_\alpha < 0.5$). Examples in each category have been identified by relative values of one-point rate constants for exchange and racemization of carbon acids in a variety of solvent–base media.[3]

However, the mechanisms which produce the over-all stereochemical results of isotopic exchange are less well defined. Clearly, $k_e/k_\alpha > 1.0$ indicates that a mechanism of exchange with retention is important, but other mechanisms are competitive because the limiting k_e/k_α value of infinity has never been attained. Similarly, $k_e/k_\alpha < 0.5$ indicates that an isoinversion (inversion without exchange) mechanism is important, but the limiting k_e/k_α value of zero has never been attained. More ambiguous is $k_e/k_\alpha = 1.0$, a result that could be ascribed to a combination of retention and inversion mechanisms as well as a total racemization mechanism. The wealth of examples of $k_e/k_\alpha = 1.0$ now in the literature makes it unlikely that more than a small fraction of them are due to a fortuitous combination of mechanisms. Most ambiguous is $0.5 \leq k_e/k_\alpha < 1.0$, a result that could be due to any of several combinations of two or more mechanistic pathways. In all reported base-catalyzed hydrogen–deuterium exchange reactions that occurred with some stereospecificity, there were processes competing with the one which caused the net stereochemical result.[3]

The solvent and base employed have a profound influence on the course of isotopic exchange. Exchange of (−)-2-(N,N-dimethylcarboxamido)-9-methylfluorene-9-d (I-D_-) proceeded with net retention with amine and potassium alkoxide bases in the relatively nonpolar solvents t-butyl alcohol, benzene, phenol, and tetrahydrofuran.[4] Isoracemization of (+)-2-(N,N-dimethylcarboxamido)-7-nitro-9-methylfluorene-9-d (II-D_+) and of (+)-2-phenylbutyronitrile-2-d (III-D_+) occurred in t-butyl alcohol and in t-butyl alcohol–tetrahydrofuran mixtures with tri-n-propylamine as base.[5] The intermediate near-planar carbanions were said to exist in the form of ion pairs when amines were used as bases, or in the form of hydrogen-bonded anions when alkoxides were used as bases. In either case the mechanistic intermediates involved in isoracemization and exchange with retention were thought to be highly structured because of low solvent polarity. In contrast, exchange of
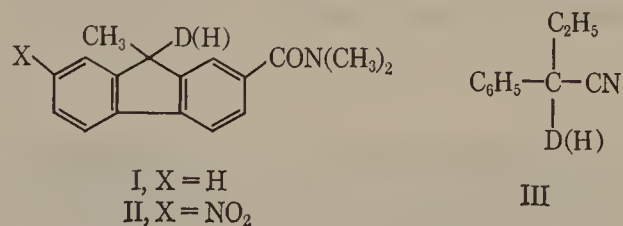
I-D_- with total racemization occurred in relatively polar solvents, ethylene glycol, methanol, and dimethyl sulfoxide, with alkoxides and ammonia as bases.[4] The total racemization was attributed to the ability of polar solvents to disperse charge and consequently promote destruction of asymmetrically solvated carbanionic species.[4]

A mechanism of inversion with exchange was assigned to exchange of I-D_- with tri-n-propylamine in methanol and with potassium methoxide in methanol.[4] The

(3) For a review, see D. J. Cram, "Fundamentals of Carbanion Chemistry," Academic Press Inc., New York, N. Y., 1965, Chapter 3.
(4) D. J. Cram and L. Gosser, J. Am. Chem. Soc., 86, 5445 (1964).
(5) D. J. Cram and L. Gosser, ibid., 86, 2950, 5457 (1964).

values of $k_e/k_\alpha \sim 0.7$ (one-point rate constants) were attributed to the ability of methanol to solvate charged species. Evidence for an inversion mechanism had previously been found in electrophilic substitutions with carbon leaving groups in polar solvents. For example, cleavage of the potassium salt of (+)-2,3-diphenyl-3-methyl-2-pentanol (IV) to 2-phenylbutane proceeded with 42% inversion of configuration in methanol,[6] and decarboxylation of salts of (−)-2-cyano-2-phenylbutyric acid (V) in ethylene glycol proceeded with 11% inversion.[7] The inversion-with-exchange mechanism for isotopic exchange was then formulated by analogy rather than with distinct experimental proof. In this paper we will show that the net inversion ($k_e/k_\alpha = 0.92$) in exchange of I-H_+ with potassium methoxide in methanol-O-d is due entirely to an intramolecular rather than an intermolecular inversion pathway in the mechanism for exchange.

IV   V
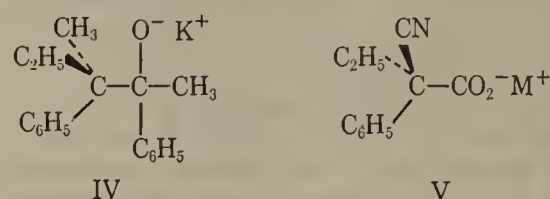
Kinetic Model for Hydrogen–Deuterium Exchange.[8] All processes which may occur during exchange of an optically active carbon acid (H_+) are defined in Chart I. In this scheme, the H or D refers to the isotope and the + or − to the sign of rotation of the carbon acid. The mechanism is identified by the rate constants: k_1 (exchange with retention), k_2 (exchange with inversion), k_3 (isoinversion), and k_4 (inversion of exchanged material). In this model, total racemization with exchange is composed of equal contributions from the processes governed by k_1 and k_2. The model assumes that ma-

Chart I. Processes Involved in Isotopic Exchange

$$H_+ \xrightarrow{k_1} D_+ \qquad\qquad H_- \xrightarrow{k_2} D_+$$

$$H_+ \xrightarrow{k_2} D_- \qquad\qquad H_- \xrightarrow{k_3} H_+$$

$$H_+ \xrightarrow{k_3} H_- \qquad\qquad D_+ \xrightarrow{k_4} D_-$$

$$H_- \xrightarrow{k_1} D_- \qquad\qquad D_- \xrightarrow{k_4} D_+$$
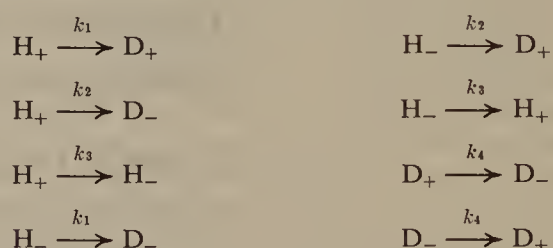
terial once deuterated never is reprotonated. If solvent contains more than 99% deuterium at its exchangeable positions, then the protons lost by substrate become drowned in the large deuterium pool. Equations 1–4 are the first-order rate expressions resulting from our definition of the model, where [H_+] represents the mole fraction of protio dextrorotatory material in the substrate. The simultaneous differential eq 1–4 are solved to give eq 5–8 which express the concentrations of each species in the substrate mixture in terms of rate constants and time, and where $\beta = k_1 + k_2$ and $\gamma = k_1 + k_2 + 2k_3 = \beta + 2k_3$.

$$d[H_+]/dt = -(k_1 + k_2 + k_3)[H_+] + k_3[H_-] \quad (1)$$

$$d[H_-]/dt = -(k_1 + k_2 + k_3)[H_-] + k_3[H_+] \quad (2)$$

$$d[D_+]/dt = k_1[H_+] + k_2[H_-] + k_4[D_-] - k_4[D_+] \quad (3)$$

(6) D. J. Cram, A. Langemann, and F. Hauck, ibid., 81, 5750 (1959).
(7) D. J. Cram and P. Haberfield, ibid., 83, 2354 (1961).
(8) Further details of the derivation are available from E. W. G.

Table I. Racemization and Exchange Kinetics of 0.060 M I-H(D)$_+$ in Methanol-O-$d(h)^a$ with Potassium Methoxide at 24.9 $\pm$ 0.1°

Run	Subst	Solv	[KOCH$_3$], M	Process	$k_1 \times 10^5$, sec^{-1} ^{b}	$k_2 \times 10^4$, l. mole^{-1} sec^{-1} ^{c}
1	H	H	0.0412	Racemization^d	12.01 $\pm$ 0.01	29.2 $\pm$ 0.3
2	H	H	0.0730	Racemization^d	21.2 $\pm$ 0.1	28.9 $\pm$ 0.3
3	H	H	0.0961	Racemization^d	27.6 $\pm$ 0.1	28.7 $\pm$ 0.3
4	D	H	0.0794	Racemization^d	3.44 $\pm$ 0.01	4.34 $\pm$ 0.13
5	D	D	0.0777	Racemization^d	7.86 $\pm$ 0.01	10.12 $\pm$ 0.11
6	H	D	0.0739	Racemization^d	48.5 $\pm$ 0.6	65.7 $\pm$ 1.5
7	H	D	0.0589	Exchange^e	36.4 $\pm$ 0.8	61.8 $\pm$ 2.0
8	D	H	0.0726	Exchange^e	2.59 $\pm$ 0.07	3.57 $\pm$ 0.13

^{a} CH$_3$OD used contained greater than 0.99 atom of D per molecule. ^{b} First-order rate constants and their standard deviations were calculated by a least-squares computer program, for which we thank Dr. Paul Haake. ^{c} Second-order rate constants reported are first-order constants divided by base concentration. Estimated error was obtained by the method of total differentials assuming a 1% error in base concentration. ^{d} Racemizations were followed at 436 mμ; 25–50 points were taken in each run. ^{e} Deuterium analyses were carried out by infrared spectrophotometry; 6–8 points were taken in each run.

$$d[D_-]/dt = k_1[H_-] + k_2[H_+] + k_4[D_+] - k_4[D_-] \quad (4)$$

$$[H_+] = \frac{1}{2}[e^{-\beta t} + e^{-\gamma t}] \quad (5)$$

$$[H_-] = \frac{1}{2}[e^{-\beta t} - e^{-\gamma t}] \quad (6)$$

$$[D_+] = \frac{1}{2}\left[(1 - e^{-\beta t}) - \left(\frac{k_2 - k_1}{\gamma - 2k_4}\right)(e^{-2k_4 t} - e^{-\gamma t})\right] \quad (7)$$

$$[D_-] = \frac{1}{2}\left[(1 - e^{-\beta t}) + \left(\frac{k_2 - k_1}{\gamma - 2k_4}\right)(e^{-2k_4 t} - e^{-\gamma t})\right] \quad (8)$$

Equations 5–8 are used to solve for rate constants k_1, k_2, and k_3 in terms of reaction time t, an independently measured k_4, and the concentrations of the four components of a partially exchanged and racemized carbon acid. Combination of eq 5–6 gives eq 9. Solu-

$$k_3 = \frac{1}{2t} \ln\left[\frac{([H_+]/[H_-]) + 1}{([H_+]/[H_-]) - 1}\right] \quad (9)$$

$$(k_1 + k_2) = \beta = \frac{1}{t} \ln\left[\frac{(1 + e^{-2k_3 t})}{2[H_+]}\right] \quad (10)$$

$$(k_2 - k_1) = \frac{([D_-] - [D_+])(\gamma - 2k_4)}{(e^{-2k_4 t} - e^{-\gamma t})} \quad (11)$$

$$k_1 = \frac{1}{2}[\beta - (k_2 - k_1)] \quad (12)$$

$$k_2 = \frac{1}{2}[\beta + (k_2 - k_1)] \quad (13)$$

tion of eq 5 gives eq 10 for β. Combination of eq 7–8 gives eq 11. Solutions for rate constants k_1 and k_2 are obtained by combination of eq 10–11 to give eq 12–13. Hence, one method of calculating the rate constants for the mechanistic components of isotopic exchange involves determination of the isotopic and enantiomeric composition of a partially exchanged and racemized carbon acid.

Another method of calculating k_1, k_2, and k_3 involves only kinetic measurements. Equation 14 expresses the rotation of a solution of an optically active carbon acid in terms of α_0 (its rotation at zero time) and the mole fractions of each component. Substitution of eq 5–8 into eq 14 gives eq 15, where $\phi = k_4/(k_2 + k_3)$ (the

reciprocal of the kinetic isotope effect k_H/k_D for racemization), $\psi = (k_2 - k_1)/2(k_2 + k_3)$, and $\theta = 2(k_2 + k_3)$ (the rate constant for racemization at zero time). Measurements of the exchange rate ($k_e = \beta$), θ, and ψ permit evaluation of rate constants k_1, k_2, and k_3. Only when $\phi = 1$ (no isotope effect) or $\psi = 0$ ($k_2 = k_1$) does α exhibit simple first-order decay. For all cases where $\phi \neq 1$ and $\psi \neq 0$, ψ can be determined from eq 15 by a method of successive approximations if sufficiently accurate data on rotation as a function of time are available.

$$\alpha = \alpha_0([H_+] + [D_+] - [H_-] - [D_-]) \quad (14)$$

$$\alpha = \left[\frac{\alpha_0}{(\phi - 1) + \psi}\right][(\phi - 1)e^{-\theta(1-\psi)t} + \psi e^{-\theta\phi t}] \quad (15)$$

When $\phi < 1$ (normal isotope effect) and $\psi > 0$ (exchange with net inversion), a faster reacting protio compound is converted to a slower reacting deuterio compound of opposite rotation. As a result, the observed sign of rotation of a reacting solution should change at some time during the run as shown in Figure 1. If the isotope effect and the rate constant for racemization at zero time are known, the function ψ may be calculated from the time at which the observed rotation equals zero, t_x, or from the time at which the rotation reaches a minimum, t_m. As a result, the rate constants k_1, k_2, and k_3 may be calculated directly if $\phi < 1$ and $\psi \geq 0$.

Results

Kinetics of Racemization and Exchange of I-H(D) in Methanol-O-$d(h)$. Racemization and hydrogen–deuterium exchange rate constants with all possible isotopic combinations for I-H(D) in methanol-O-$d(h)$ with potassium methoxide at 24.9° are reported in Table I. The constant value obtained for second-order rate constants in runs 1–3 indicates that racemization is first order in potassium methoxide over the range of base concentrations employed. A large substrate isotope effect ($k_H/k_D = 6.6$) and a substantial solvent isotope effect ($k^{CH_3OD}/k^{CH_3OH} = 2.3$) were found for racemization. Although exchange occurred with net inversion with both combinations of solvent and substrate isotopes, the exchange of I-D$_+$ in methanol-O-h was the more stereospecific. These isotope effects are reported in Table II.

Rate Constants for Mechanistic Components. Kinetic Method. Application of the kinetic method of the

Figure 1. Observed rotation as a function of time for $\phi = 0.154$, $\psi = 0.18$, and $\theta = 4.85 \times 10^{-4}$ sec^{-1}.

model has enabled calculation of the rate constants for exchange with retention (k_1), exchange with inversion (k_2), and isoinversion (k_3) in the isotopic exchange of I-H$_+$ in methanol-O-d. Racemization was a simple first-order process, and no negative rotation was ever observed during run 6. Since there was a large hydrogen–deuterium isotope effect ($\phi = 0.15$), in terms

Table II. Rate Ratios for Racemization and Exchange of 0.060 M I in Methanol with 0.07–0.08 M Potassium Methoxide at 24.9°

$(k_H CH_3OH/k_D CH_3OH)^a$	6.66 ± 0.27^d
$(k_H CH_3OD/k_D CH_3OD)^{a,b}$	6.50 ± 0.22^d
$(k_H CH_3OD/k_H CH_3OH)^{b,c}$	2.27 ± 0.07^d
$(k_D CH_3OD/k_D CH_3OH)^{b,c}$	2.33 ± 0.10^d
k_e/k_α (I-H in CH$_3$OD)^b	0.92 ± 0.05^e
k_e/k_α (I-D in CH$_3$OH)	0.82 ± 0.05^d

^{a} Substrate kinetic isotope effect for racemization. ^{b} CH$_3$OD used contained greater than 0.99 atom of D per molecule. ^{c} Solvent isotope effect for racemization. ^{d} Ratios of second-order rate constants. Errors represent standard deviations. ^{e} A mean value from two experiments: ratio of second-order rate constants from Table I = 0.94 ± 0.05, and ratio of first-order rate constants from an independent run = 0.90 ± 0.05.

Table III. Comparison of Rate Constants for Mechanistic Components of Base-Catalyzed Hydrogen–Deuterium Exchange and Racemization of I at 24.9°

Constant	I-H$_+$ in CH$_3$OD with CH$_3$OK ——10^{3}k, l. mole^{-1} sec^{-1}—— Kinetic^a	Resolution^b	I-D$_+$ in (CH$_3$)$_3$COH with C$_6$H$_5$OK^c 10^{6}k, sec^{-1}
k_1	3.02 ± 0.17^d	2.80 ± 0.46	12.1 ± 4.4
k_2	3.02 ± 0.17	2.99 ± 0.46	5.6 ± 4.4
k_3	0.26 ± 0.17	0.26 ± 0.05	0.46 ± 0.05
$k_4{}^e$	0.51 ± 0.01	0.51 ± 0.01	44.8 ± 0.8^f

^{a} Second-order rate constants from kinetic data. ^{b} Second-order rate constants from reresolution data. A solution of 0.060 M I-H$_+$ and 0.069 M potassium methoxide in methanol-O-d (greater than 0.99 atom of D per molecule) was racemized to 44.2% of its original rotation before resolution. ^{c} First-order rate constants from the reresolution method. A solution of 0.13 M I-D$_+$ (0.97 atom of D per molecule), 0.081 M potassium phenoxide, and 0.014 M phenol in t-butyl alcohol was racemized to 49.0% of its original rotation before resolution. ^{d} Errors represent standard deviations. ^{e} Independently measured. ^{f} Calculated from a run containing 0.13 M I-H$_+$, 0.1074 M potassium phenoxide, and 0.0095 M phenol in t-butyl alcohol by assuming that racemization is first order in base, and that the rate is not affected by small changes in phenol concentration.

Table IV. Dependence of Rotation on ψ

ψ	$10^{-3}t_x$, sec	$10^{-4}t_m$, sec	α_m, deg
0.50	3.13	1.02	−0.425
0.18	4.8	1.00	−0.093
0.05	7.3	1.21	−0.019
0.01	11.0	1.56	−0.003

of the model, $\psi = 0$. Calculated rate constants k_1, k_2, and k_3 are reported in Table III. Net inversion with exchange ($k_2 > k_1$) would cause the rotation during this kinetic run to become negative. If the rotation ever becomes negative, it must pass through zero at some time t_x (see Figure 1). This occurs when the exponential term of eq 15 equals zero. Solution of eq 15 for t_x gives eq 16, which was used to calculate values of t_x expected for hypothetical values of ψ. The time at which the rotation is a minimum, t_m of Figure 1, may be calculated from eq 17, which was obtained from eq 15 by equating the first derivative of α with respect to t to zero and solving for t. Substitution of t_m into eq 15 provided values for the minimum rotation, α_m, which could be observed for a given value of ψ under the experimental conditions used in run 6 ($\theta = 4.85 \times 10^{-4}$ sec^{-1}, $\phi = 0.154$, $\alpha_0 +0.904°$). These calculations of t_x, t_m, and α_m are reported in Table IV. The calculated

$$t_x = \left[\frac{1}{\theta(1 - \psi - \phi)} \right] \ln (1 - \phi)/\psi \qquad (16)$$

$$t_m = \left[\frac{1}{\theta(1 - \psi - \phi)} \right]\left[\frac{\ln (1 - \phi)(1 - \psi)}{\phi\psi} \right] \qquad (17)$$

value of α_m −0.003° for $\psi = 0.01$ is greater than experimental error on the polarimeter used for kinetic runs. Assuming the polarimeter was accurate to 0.001°, a calculation of ψ was made by taking the time t_x to be that time during run 6 at which the polarimeter first read 0.000°. That calculation indicated a difference between k_1 and k_2 of only 0.2% of their mean value. Therefore, $k_1 = k_2$ within experimental error.

Reresolution Method. Rate constants k_1, k_2, and k_3 were calculated for exchange of I-H$_+$ in methanol-O-d with potassium methoxide and exchange of I-D$_+$ in t-butyl alcohol with potassium phenoxide using eq 9–13. The results are reported in Table III. The isotopic symbols of the model were switched when D$_+$ rather than H$_+$ served as starting material. Concentrations of the four species in partially exchanged and racemized I were determined from mass spectral deuterium analyses of the antipode and of the racemate obtained by fractional crystallization of the recovered material from acetone. This analytical method depends on the assumption that protio and deuterio compounds do not fractionate during recrystallization. An isotopic dilution experiment with another optically active carbon acid gave no isotopic fractionation,[9] indicating that this assumption is reasonable.

The rather large limits of error on k_1 and k_2 reported in Table III for the reresolution method are caused by possible errors in deuterium analyses (which were estimated to be accurate to ±0.003 atom D per molecule)

(9) D. J. Cram and T. A. Whitney, *J. Am. Chem. Soc.*, **89**, 4651 (1967).

and in the rate constant k_4, and by the uncertainty in the time due to fluctuations in temperature for the first few minutes after mixing base and substrate.

The results in Table III show good agreement between the two experimentally independent methods of calculating rate constants for the mechanistic components. The kinetic method demonstrated conclusively that in methanol with potassium methoxide exchange of I-H$_+$ occurred with no net retention or inversion, and consequently that the over-all net inversion was due entirely to a small isoinversion component. The exchange and racemization of I-D$_+$ in t-butyl alcohol with potassium phenoxide also occurred with a small isoinversion component, even though the k_e/k_α value (1.00 ± 0.05) under these conditions indicated no net stereospecificity for the exchange. Racemization of I in t-butyl alcohol also had a large substrate isotope effect, $k_H/k_D = 5.9 \pm 0.4$. Since an isoinversion component contributed to the over-all result, the exchange in t-butyl alcohol must have taken place with low net retention in order to balance the isoinversion.

Discussion

Mechanism. Scheme I may be used to explain the stereochemical courses of isotopic exchange of I-H$_+$ in methanol-O-d. Mechanisms which involve carbanions hydrogen bonded to more than one solvent molecule have been discounted because of the intramolecularity observed in this and other proton transfers. Also discounted are mechanisms which involve nonhydrogen-bonded carbanions as discrete intermediates. A more detailed discussion of singly hydrogen-bonded carbanions appears later in this paper. In Scheme I, k_b and k_g are rate constants for intramolecular

Scheme I
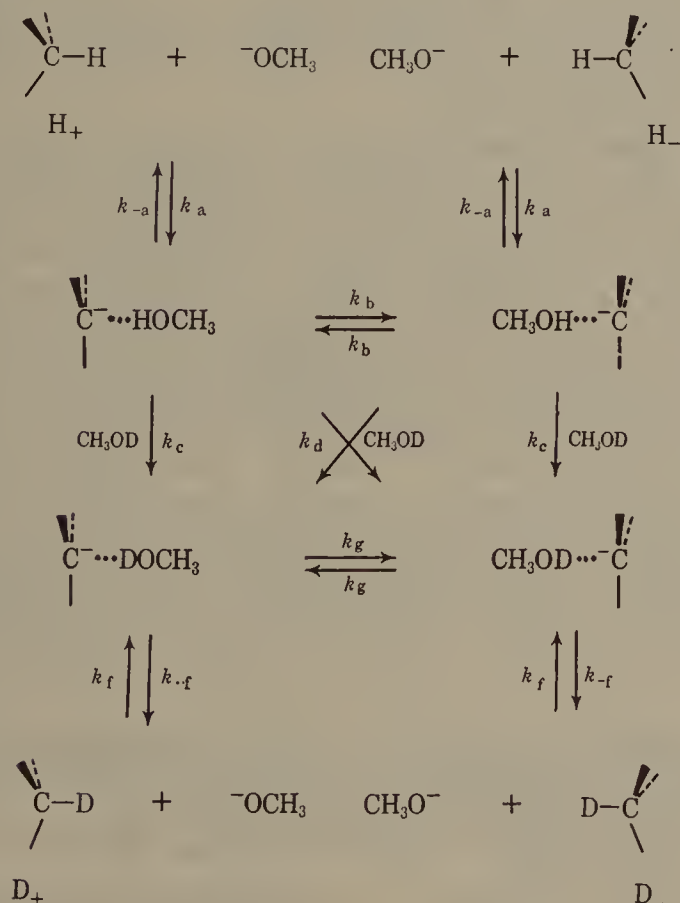
shifts of hydrogen bonds which interconvert enantiomeric hydrogen-bonded carbanions, while k_c and k_d are rate constants for exchanges of hydrogen-bonded carbanions with the solvent. When the new hydrogen bond forms on the side of the original covalent bond, k_c is the rate constant. When the new hydrogen bond forms on the opposite side, k_d is the rate constant. Processes by which deuterated material is reconverted to protonated material are neglected because the solvent always contained at least 99% deuterium at its exchangeable position.

Treatment of Scheme I by the steady-state approximation gave eq 18–23 which express the experimental rate constants, k_1, k_2, k_3, and k_4, in terms of the rate constants of the scheme.[8]

$$k_1 = k_a \frac{m(k_{-f} + k_g) + nk_g}{(k_{-f} + 2k_g)(k_{-a} + k_c + k_d)(k_{-a} + k_c + k_d + 2k_b)} \quad (18)$$

$$k_2 = k_a \frac{n(k_{-f} + k_g) + mk_g}{(k_{-f} + 2k_g)(k_{-a} + k_c + k_d)(k_{-a} + k_c + k_d + 2k_b)} \quad (19)$$

$$m = k_c(k_{-a} + k_c + k_d + 2k_b) + k_b(k_d - k_c) \quad (20)$$

$$n = k_d(k_{-a} + k_c + k_d + 2k_b) - k_b(k_d - k_c) \quad (21)$$

$$k_3 = \frac{k_a k_{-a} k_b}{(k_{-a} + k_c + k_d)(k_{-a} + k_c + k_d + 2k_b)} \quad (22)$$

$$k_4 = \frac{k_g k_f}{(k_{-f} + 2k_g)} \quad (23)$$

When $k_1 = k_2$, as with I-H$_+$ in methanol-O-d, eq 18 and 19 require that either $k_c = k_d$ or $k_b \gg k_{-a}$, k_c, or k_d. These possibilities require examination.

If $k_c = k_d$, the carbanions exchange one tightly bound solvent molecule for another without regard for the face of the planar carbanion with which the original methanol molecule was associated. Experimentally, intramolecular shift of hydrogen bonds (k_b) must be competitive with intermolecular exchange of hydrogen bond donors (k_c and k_d) to account for the isoinversion component. One special case of $k_c = k_d$ involves $k_{-a} \gg k_b$, k_c, or k_d. In other words, the rate-determining steps for racemization are governed by k_b, k_c, and k_d. Simplification of eq 18–22 through use of $k_c = k_d$ and $k_{-a} \gg k_b$, k_c, or k_d gives $k_e/k_\alpha = k_c/(k_b + k_c) = 0.92$, or $k_c = 11.6k_b$. On the other hand, if $k_b \gg k_{-a}$, k_c, or k_d, simplification of eq 18–22 gives $k_\alpha = k_a$ and $k_e/k_\alpha = (k_c + k_d)/(k_{-a} + k_c + k_d) = 0.92$, or $(k_c + k_d) = 11.6k_{-a}$. Although this latter possibility appears intuitively less likely than the former, it can better explain the large substrate isotope effect on racemization of I in methanol with potassium methoxide.

Substrate Isotope Effect. In the model of Table V, the ground states and the rate-determining transition states for racemization of I in methanol are formulated for two cases: where k_b is very large; and where k_{-a} is very large. In the ground states of Table V, the methoxide ion is strongly hydrogen bonded to one methanol molecule. If $k_b \gg k_{-a}$, k_c, or k_d, the initial proton abstraction is rate determining, and the transition state contains no covalent bond, a partial C$\cdots$H$\cdots$O bond, and a partial O$\cdots$H hydrogen bond. For loss of a covalent bond, a large primary isotope effect is expected. On the other hand, the model transition state for $k_{-a} \gg k_b$, k_c, and k_d contains two nearly

Table V

Substrate and solvent	Ground state	Transition states	
		$k_b \gg k_{-a}, k_c,$ and k_d	$k_{-a} \gg k_b, k_c,$ and k_d
I-H in CH₃OH	$\begin{array}{c} \text{HOCH}_3 \\ \mid \\ -\overset{\mid}{\text{C}}-\text{H} \ + \ ^-\text{OCH}_3 \\ \mid \end{array}$	$\left[\begin{array}{c} \text{HOCH}_3 \\ \mid \\ -\text{C}\cdots\text{H}\cdots\text{OCH}_3 \\ \mid \end{array}\right]^-$	$\left[\begin{array}{c} \mid \quad \diagup\text{HOCH}_3 \\ -\text{C}\diagdown \\ \mid \quad \diagdown\text{HOCH}_3 \end{array}\right]^-$
I-D in CH₃OH	$\begin{array}{c} \text{HOCH}_3 \\ \mid \\ -\overset{\mid}{\text{C}}-\text{D} \ + \ ^-\text{OCH}_3 \\ \mid \end{array}$	$\left[\begin{array}{c} \text{HOCH}_3 \\ \mid \\ -\text{C}\cdots\text{D}\cdots\text{OCH}_3 \\ \mid \end{array}\right]^-$	$\left[\begin{array}{c} \mid \quad \diagup\text{HOCH}_3 \\ -\text{C}\diagdown \\ \mid \quad \diagdown\text{DOCH}_3 \end{array}\right]^-$
I-H in CH₃OD	$\begin{array}{c} \text{DOCH}_3 \\ \mid \\ -\overset{\mid}{\text{C}}-\text{H} \ + \ ^-\text{OCH}_3 \\ \mid \end{array}$	$\left[\begin{array}{c} \text{DOCH}_3 \\ \mid \\ -\text{C}\cdots\text{H}\cdots\text{OCH}_3 \\ \mid \end{array}\right]^-$	$\left[\begin{array}{c} \mid \quad \diagup\text{DOCH}_3 \\ -\text{C}\diagdown \\ \mid \quad \diagdown\text{HOCH}_3 \end{array}\right]^-$

covalent O–H bonds and two partial O $\cdots$ H hydrogen bonds. Only a small primary isotope effect could be expected when there is little loss of stretching vibration in the transition state. In other words, the over-all isotope effect for large k_{-a} is the product of an equilibrium isotope effect and a kinetic isotope effect for exchange of hydrogen-bond donors expressed by eq 24.[10]

$$\frac{k_H}{k_D} = \frac{k_a^H k_{-a}^D k_c^H}{k_a^D k_{-a}^H k_c^D} = \frac{K_{eq}^H k_c^H}{K_{eq}^D k_c^D} \tag{24}$$

Although the transition state for rate constant k_c is used in Table V, that for k_d would provide the same conclusions.

It is not clear what maximum primary isotope effects are. Two statistical mechanical models provide maximum isotope effects of $k_H/k_D = 6.9$ and $k_H/k_D = 13$ for abstraction of hydrogen from carbon at 25° in the absence of proton tunneling.[11] Streitwieser and coworkers have reported deuterium–tritium isotope effects as high as $k_D/k_T = 2.9$ for isotopic exchange of toluene and ethylbenzene in cyclohexylamine with lithium cyclohexylamide.[12] When converted to hydrogen–deuterium isotope effects by the equation of Swain and co-workers,[13] $k_D/k_T = 2.9$ becomes $k_H/k_D = 12$, the highest isotope effect for abstraction of hydrogen from carbon in the absence of tunneling of which we are aware. The authors concluded that in isotopic exchange of toluene, hydrogen abstraction was rate determining, and the carbanion, once formed, was never reconverted to starting material.

An alternative to the prerate-determining equilibrium explanation[10] for low primary hydrogen–deuterium isotope effects has been presented by Westheimer[14] and modified by Bell.[15] They contend that a maximum isotope effect is observed only when the hydrogen atom or ion being transferred is symmetrically located in the transition state between the atom to which it was covalently bonded and the atom to which a covalent bond is forming. In nonsymmetrical transition states,

C $\cdots$ H $\cdots$ O stretching vibrations which involve motion of the hydrogen atom reduce the isotope effect. This approach has been used to explain the base strength dependence of isotope effects for hydrogen abstraction.[13,15] For example, the zero-order bromination of nitromethane catalyzed by water has $k_H/k_D = 3.8$, but catalyzed by hydroxide ion has $k_H/k_D = 9.6$.[15a] Isotope effects are maximized when the carbon acid and the conjugate acid of the basic catalyst have the same pK_a.[15b]

In previous work both the prerate-determining equilibrium approach[10,16] and the nonsymmetrical transition state approach[15,17] have been used to explain low primary isotope effects in carbanion-forming hydrogen abstractions. In the present work, both effects might reduce the isotope effect from a maximum value (attainable only if k_{-a} of Scheme I was negligibly valued, and the pK_a of the conjugate acid of the alkoxide catalyst was the same as that of the substrate) to the observed $k_H/k_D = 6.6$. The presence of an isoinversion component in the mechanism requires a contribution by the isotope effect for k_{-a} to the over-all isotope effect. A difference of 6–7 units in the pK_a values of I and methanol provides further reduction from the maximum. The isotope effects reported here agree well with previous values for sodium methoxide catalyzed exchange of fluorene in methanol ($k_D/k_T = 2.2$ or $k_H/k_D = 6$) from the Swain equation[13,18] and for exchange of fluorene in liquid ammonia ($k_D/k_T = 1.9$).[19]

The large isotope effect ($k_H/k_D = 6.6$) for racemization of I in methanol with potassium methoxide makes $k_{-a} \gg k_b, k_c$, or k_d in Scheme I very unlikely. On the other hand, it supports the possibility that $k_b \gg k_{-a}$, k_c, or k_d because only in that case is a covalent bond broken in the rate-determining transition state for racemization. Situations where $k_c = k_d$ but k_{-a} is of the same order of magnitude as k_b, k_c, and k_d are also consistent with a large isotope effect as long as the rate-determining transition states involve considerable loss of covalent bonding.

Singly Hydrogen-Bonded Carbanions.[20] Whatever the relative values of the rate constants of Scheme I, binding between the planar delocalized carbanion and the solvent molecule formed by hydrogen abstraction must be considerably stronger than binding between the carbanion and any other solvent molecule. Otherwise, isoinversion in racemization of I-H₊ in methanol-O-d would not have been observed. A variety of intramolecular proton transfers support this "singly hydrogen-bonded carbanion" concept. Most striking is the 1,5 proton transfer converting triene VI to triarylmethane VII which occurred with 98% intramolecularity in nonpolar deuterated solvents with tertiary amine catalysts and 46% intramolecularity even in methanol-O-d with sodium methoxide catalyst.[21] Similar re-

(10) (a) D. J. Cram, C. A. Kingsbury, and B. Rickborn, *J. Am. Chem. Soc.*, 83, 3688 (1961); (b) D. J. Cram, D. A. Scott, and W. D. Nielsen, *ibid.*, 83, 3696 (1961).

(11) L. Melander, "Isotope Effects on Reaction Rates," The Ronald Press Co., New York, N. Y., 1960, p 22.

(12) (a) A. Streitwieser, Jr., W. C. Langworthy, and D. E. Van Sickle, *J. Am. Chem. Soc.*, 84, 251 (1962); (b) A. Streitwieser, Jr., D. E. Van Sickle, and L. Reif, *ibid.*, 84, 258 (1962).

(13) C. G. Swain, E. C. Stivers, J. F. Reuwer, Jr., and L. J. Schaad, *ibid.*, 80, 5885 (1958).

(14) F. H. Westheimer, *Chem. Rev.*, 61, 265 (1961).

(15) (a) R. P. Bell, *Discussions Faraday Soc.*, 39, 16 (1965); (b) R. P. Bell and D. M. Goodall, *Proc. Roy. Soc.* (London), A294, 273 (1966).

(16) (a) D. J. Cram and R. T. Uyeda, *J. Am. Chem. Soc.*, 86, 5466 (1964); (b) J. E. Hofmann, A. Schriesheim, and R. E. Nickols, *Tetrahedron Letters*, 1745 (1965).

(17) S. Andreades, *J. Am. Chem. Soc.*, 86, 2003 (1964).

(18) A. Streitwieser, Jr., and J. H. Hammons, *Progr. Phys. Org. Chem.*, 3, 57 (1965).

(19) (a) F. S. Yakushin, Yu. G. Dubinskii, E. A. Yakovleva, and A. I. Shatenshtein, *Russ. J. Phys. Chem.*, 33, 647 (1959); (b) F. S. Yakushin and A. I. Shatenshtein, *Kinetics Catalysis*, 1, 457 (1960).

(20) Although we use the term "hydrogen bond," "ion–dipole interaction" or "partial bond" would serve as well.

(21) D. J. Cram, F. Willey, H. P. Fischer, H. M. Relles, and D. A. Scott, *J. Am. Chem. Soc.*, 88, 2759 (1966).

$$
\text{VI} \xrightarrow[\text{ROD}]{\text{base}} \text{VII}
$$
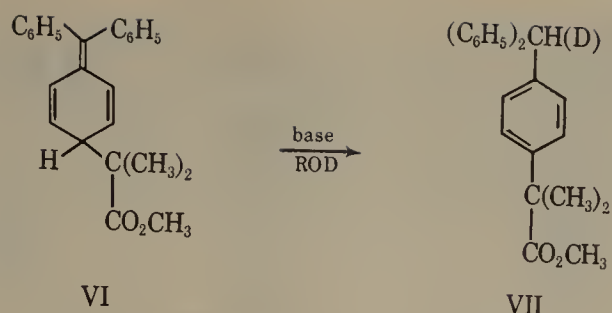
sults have been observed in base-catalyzed 1,3 proton transfers[22] and isoracemizations of carbon acids.[5,23] The energetic factors preventing strong association of the carbanion with more than one solvent molecule at a time are most likely the entropy required to form a trimeric species and the strongly hydrogen-bonded structure of the solvent.

The ability of delocalized carbanions to strongly bind to just one solvent molecule at a time implies that the negative charge in the anion may be concentrated at the carbon which is nearest that one molecule of solvent. Thus, the process defined by k_b in Scheme I might be a series of shifts of a hydrogen bond between sites in the carbanion which keeps a semilocalized negative charge at the site of hydrogen bonding. One hydrogen-bonded carbanion of I could be converted to its enantiomer by shifting the associated hydrogen from the π-electron system to a lone pair of electrons on the dimethylcarboxamido group and then to the opposite side of the planar hydrocarbon. Similar "conducted tour" mechanisms were previously formulated for isoracemization of carbon acids II and III by tri-n-propylamine in nondissociating protic solvents.[5,23]

Solvent Isotope Effect. The solvent isotope effect $(k^{CH_3OD}/k^{CH_3OH} = 2.3)$ reported for racemization of I in methanol with potassium methoxide is similar to those observed in base-catalyzed allylic isomerizations[16a,24] and in isotopic exchange of monohydrofluorocarbons in methanol with sodium methoxide.[17] Regardless of which model in Table V is used for the transition state, there is an increase in the frequency of the O–H or O–D stretching vibration of the solvent molecule as hydrogen bonding to the methoxide ion is lost. This frequency increase is greater for O–H than for O–D, causing the solvent isotope effect. Our result supports the conclusions of Swain and co-workers that OD$^-$ is a stronger base in D$_2$O than OH$^-$ is in H$_2$O, and that a reaction which proceeds by distribution of charge in the transition state will exhibit rate enhancement in heavy water.[25]

In addition to the solvent isotope effect, greater stereospecificity of exchange was observed for I-D$_+$ in methanol-O-h than for I-H$_+$ in methanol-O-d (see Table II). In terms of Scheme I, this means that either k_b is larger with I-D than with I-H, or k_c and k_d are larger with methanol-O-d than with methanol-O-h. In connection with the latter possibility, the solvent isotope effect indicates that association of methoxide and methanol-O-h is stronger than association of methoxide and methanol-O-d. Thus, methanol-O-d should be more

easily removed from solvent structure to bind with the carbanion.

Racemization in t-Butyl Alcohol. Scheme I may be applied to the isotopic exchange of I-D$_+$ in t-butyl alcohol with potassium phenoxide by interchanging the isotopic (H and D) symbols. The over-all lack of stereospecificity was due to a fortuitous combination of isoinversion, exchange with retention, and exchange with total racemization. Since exchange occurred with net retention, exchange of hydrogen-bond donors with the solvent must have taken place preferentially on one side of the carbanion such that $k_c > k_d$. Again, a large primary isotope effect ($k_H/k_D = 5.9$) indicates that k_{-a} cannot be very large relative to k_b and k_c. In order to produce the isoinversion component, k_b must be at least competitive with k_c, and $k_b \gg k_{-a}$, k_c, or k_d is a distinct possibility.

In nonpolar t-butyl alcohol, the mechanism probably involves ion pairs rather than solvated carbanions. The phenol molecule formed by proton abstraction probably associates with a solvated potassium ion, which rotates and returns another solvent molecule to the carbanion. Similar explanations have been invoked for other hydrogen–deuterium exchanges occurring with retention in nonpolar solvents.[4]

This paper has reported distinct experimental proof for isoinversion contributions to the over-all mechanisms of exchange of I-H$_+$ in methanol-O-d with potassium methoxide and I-D$_+$ in t-butyl alcohol with potassium phenoxide. However, in both media the predominant mechanistic course was total racemization with exchange indicated by large contributions from both k_1 and k_2 in our kinetic model. Experimental proof for net exchange with inversion has been found in a cyclic sulfone[9] but remains undiscovered in optically active 9-methylfluorene derivatives.

Experimental Section

Materials. Preparation of optically active and deuterated 2-(N,N-dimethylcarboxamido)-9-methylfluorene (I) has been described previously.[4] In this work, I-H$_+$ had mp 126.5–127°,[26] $[\alpha]^{25}_{546}$ +31.2°, $[\alpha]^{25}_{436}$ +60.3° (c 1.5, methanol), and $[\alpha]^{25}_{546}$ +33.4° (c 1.2, dioxane); while I-D$_+$ had mp 127–127.5°,[26] $[\alpha]^{25}_{546}$ +32.0°, $[\alpha]^{25}_{436}$ +61.8° (c 1.5, methanol), $[\alpha]^{25}_{546}$ +33.7° (c 1.1, dioxane), and contained 0.97 atom of excess D per molecule by combustion and falling drop analyses.[27] Rotations were accurate to ±0.4° under these conditions and were not concentration dependent.

Methanol was purified by the method of Fieser[28] and distilled onto molecular sieves. Methanol-O-d was prepared by hydrolysis of dimethyl carbonate in deuterium oxide according to Streitwieser and co-workers[29] and purified by the method of Fieser.[28] After distillation, it was stored in a dry nitrogen atmosphere. It contained 0.994 atom of excess D per molecule by falling drop analysis[27] and greater than 0.99 atom of excess D per molecule by nmr analysis of the hydroxyl protons and the ^{13}C satellite of the methyl group. Both methanol-O-h and methanol-O-d contained less than 0.03 wt % water by Karl Fischer titration. t-Butyl alcohol was distilled from and collected over molecular sieves. Phenol (Matheson reagent) was distilled at 0.1 mm. A small center cut with bp 42–43° was collected and stored under dry nitrogen.

Typical Racemization Rate Determination (Run 5). All glassware except the polarimeter cell used in kinetic experiments was cleaned with chromic acid, rinsed with distilled water and dilute ammonia,

(22) Reference 3, pp 175–193.
(23) Reference 3, pp 98–103.
(24) (a) D. H. Hunter and D. J. Cram, *J. Am. Chem. Soc.*, **86**, 5478 (1964); (b) S. W. Ela and D. J. Cram, *ibid.*, **88**, 5791 (1966).
(25) (a) C. G. Swain, A. D. Ketley, and R. F. W. Bader, *ibid.*, **81**, 2353 (1959); (b) C. G. Swain and R. F. W. Bader, *Tetrahedron*, **10**, 182 (1960).

(26) Melting points were taken with a Mel-Temp apparatus and are uncorrected.
(27) Performed by Josef Nemeth, Urbana, Ill.
(28) L. F. Fieser, "Experiments in Organic Chemistry," 3rd ed, D. C. Heath and Co., Boston, Mass., 1957, p 286.
(29) A. Streitwieser, Jr., L. Verbit, and P. Stang, *J. Org. Chem.*, **29**, 3706 (1964).

dried in an oven for at least 12 hr at 120°, and stored in a desiccator over phosphorus pentoxide. The polarimeter cell was cleaned in the same manner and dried with a stream of purified nitrogen for 15 min.

Into a 2-ml volumetric flask was weighed 30.0 mg of I-D$_+$. Approximately 1.5 ml of methanol-O-d was added, and the solution was thermostated at 24.8°. After 30 min, 0.20 ml of a 0.64 M potassium methoxide in methanol-O-d solution and 0.3 ml of methanol-O-d were added to the 2.00-ml mark. The solution was thoroughly mixed and 1 ml was transferred to a 1-dm polarimeter cell thermostated at 24.8°. Change in rotation was observed at the 436-mμ Hg line on a Perkin-Elmer Model 141 polarimeter.

Potassium methoxide concentration was determined by titration of four aliquots of the kinetic solution to the phenolphthalein end point with 0.01234 N hydrochloric acid to give concentrations in the range 0.0772–0.0780 M with an average of 0.0777 M. Aliquots were measured by a calibrated 0.5-ml Hamilton syringe fitted with Chaney adapter. Graphical analysis of the polarimetric data gave a first-order rate constant of 7.92×10^{-5} sec^{-1}. Least-squares computer analysis[30] of 36 data points gave a first-order constant with standard deviation of $7.86 \pm 0.01 \times 10^{-5}$ sec^{-1} and a second-order constant of $1.012 \pm 0.011 \times 10^{-3}$ l. mole^{-1} sec^{-1} assuming an error of $\pm 1.0\%$ in base concentration.

Run 6. All procedures except the collection of data were the same as in run 5 Rotation data were recorded continuously by a recorder connected to the polarimeter No significant deviation from simple first-order kinetics was noticed. After 300 min, the rotation reached 0.000° and wavered over a range of only 0.001° for an additional 90 min. This precision was better than that claimed by the manufacturer of the polarimeter. Clearly, no negative rotation was observed. Representative points from the recorder chart were used to obtain the least-squares first-order rate constant. The recorder was used to collect part or all of the data in some of the other kinetic runs as well.

Typical Exchange Rate (Run 7). In a clean, dry, 25-ml flask were placed 224.8 mg of I-H$_+$ and 13.50 ml of methanol-O-d. After 30 min at 24.8°, 1.50 ml of 0.64 N potassium methoxide in methanol-O-d was added. The solution was mixed and stoppered with a septum cap. Aliquots of 1.6 ml each were withdrawn with a nitrogen-filled syringe and quenched in 5 ml of 2 N hydrochloric acid. The acidic solution was extracted with two small portions of ether. The ether solutions were washed with water, dried over magnesium sulfate, and evaporated to an oily solid which crystallized when pentane was evaporated from it. After further drying under vacuum the samples were analyzed for deuterium by quantitative infrared measurements of a band at 1147 cm^{-1}.[4] Deuterium content and time data are summarized in Table VI. Base concentration and rate constants were determined by the methods used for racemization rates.

Table VI

Time, min	% excess D	Time, min	% excess D
6.1	23	40.2	63
14.8	36	50.4	70
23.3	45	61.4	76
31.8	53	74.6	82

k_e/k_α **for I-H$_+$ in Methanol-O-d.** A flask containing 150 mg of I-H$_+$ and 6.5 ml of methanol-O-d was thermostated at 24.9°. After 30 min, 0.25 ml of 0.65 M potassium methoxide in methanol-O-d and more methanol-O-d were added to give a total of 7.00 ml. After mixing, 1.00 ml of the solution was pipetted into each of six septum-capped test tubes and held at 24.9°. Each aliquot was quenched by addition of 0.250 ml of 1 N hydrochloric acid in methanol–water. Rotations of the quenched solutions were measured at 436 mμ. Solid I was recovered from each aliquot and analyzed for deuterium by the method described for run 7.[4] The analytical data are summarized in Table VII. The α_{obsd} at time zero was calculated from the concentration and specific rotation of I-H$^+$ in methanol. Least-squares analysis of the data gave $k_e = 1.30 \pm 0.06 \times 10^{-4}$ sec^{-1} and $k_\alpha = 1.44 \pm 0.03 \times 10^{-4}$ sec^{-1}. Thus, $k_e/k_\alpha = 0.90 \pm 0.05$. The k_e/k_α value in Table II (0.92 $\pm$ 0.05) is the mean of this result and a ratio of second-order constants from Table I.

(30) We thank Dr. Paul Haake for use of a least-squares program.

Table VII

Time, min	α_{obsd}, deg	% excess D
0.0	1.034	0
29.4	0.751	30
44.1	0.614	35
76.1	0.509	44
99.7	0.420	54
124.3	0.343	63
148.4	0.279	70

Partial Exchange of I-H$_+$ in Methanol-O-d. A solution containing 750 mg of I-H$_+$ in 40 ml of methanol-O-d was thermostated at 24.8°. After 15 min, 6.0 ml of a 0.65 M potassium methoxide solution and more methanol-O-d were added to the 50-ml mark. After thorough mixing, 1 ml of the solution was transferred to a thermostated polarimeter cell. When the rotation reached 0.400° at 436 mμ (compared to 0.904° for the same concentration of unracemized I-H$_+$ in methanol), the solution was quenched with 250 ml of 2 N hydrochloric acid. Two aliquots from the polarimeter cell were titrated as described in run 5 to give a potassium methoxide concentration of 0.069 M. The quenched mixture was extracted with three 150-ml portions of ether. The combined ether solutions were washed with water, dried over magnesium sulfate, and evaporated to 695 mg (95%) of dry, white solid A.

Reresolution of Partially Racemized I. All fractional crystallizations were carried out in reagent grade acetone Rotations were taken in dioxane at 546 mμ and 25°. Recrystallization of solid A gave 398 mg of solid B, having $[\alpha]$ +8.2° (c 1.1). From the mother liquors of B, 292 mg of solid C, having $[\alpha]$ +24.0° (c 1.05), was recovered. Solid B gave 257 mg of solid D, having $[\alpha]$ +1.8° (c 1.0). Solid D gave 149 mg of solid E, having $[\alpha]$ +0.4° (c 1.7). Solid C gave 153 mg of solid F, having $[\alpha]$ +30.3° (c 1.2). Solid F gave 85 mg of solid G, having $[\alpha]$ +32.3° (c 1.15). Solids E and G contained 0.642 and 0.361 atom excess D per molecule, respectively, by mass spectrometry.

Partial Exchange of I-D$_+$ in t-Butyl Alcohol. Clean, freshly cut potassium, 79.3 mg, was dissolved in a solution of 0.21 mg of phenol in 17.0 ml of t-butyl alcohol. In another flask, 811 mg of I-D$_+$ was dissolved in 8.0 ml of t-butyl alcohol. After 15 min at 24.9°, the two solutions were combined to give a solution 0.13 M in I-D$_+$, 0.081 M in potassium phenoxide, and 0.014 M in phenol. After thorough mixing, 1 ml of the solution was transferred to a thermostated polarimeter cell. When the rotation reached 0.454° at 546 mμ (compared to 0.926° for the same concentration of I-D$_+$ in t-butyl alcohol) after 635 min, the solution was quenched with 200 ml of 2 N hydrochloric acid. The solid was recovered as previously described. A 30-g column of silica gel was prepared in 20% ether in pentane. The solid was placed on the column in a minimal amount of benzene and eluted with ether. Mass spectral analysis of the recovered solid J showed 0.469 atom excess D per molecule. The rotation and deuterium content of J provided a one-point k_e/k_α value of 1.00 $\pm$ 0.05. Fractional crystallizations starting with J were carried out by the method described above to give solid K, having $[\alpha]^{25}_{546}$ +33.6° (c 1.1, dioxane), and solid L, having $[\alpha]^{25}_{546}$ +1.6° (c 1.6, dioxane). Solids K and L contained 0.627 and 0.346 atom excess D per molecule, respectively, by mass spectral analysis.

Racemization Rate of I-H$_+$ in t-Butyl Alcohol with Potassium Phenoxide. In a 1-ml volumetric flask were placed 11.0 mg of phenol and 0.17 ml of 0.5 M potassium t-butoxide in t-butyl alcohol solution. In another flask, 32.4 mg of I-H$_+$ was dissolved in 0.5 ml of t-butyl alcohol. After 15 min at 24.9°, the substrate solution and more t-butyl alcohol were added to the base to give 1.00 ml of solution, which was thoroughly mixed and transferred to a polarimeter cell thermostated at 24.9°. Change of rotation was followed at 546 mμ. Titration of two aliquots to the brom cresol green end point with 0.01234 N hydrochloric acid determined the base concentration, 0.1074 M, and by difference the phenol concentration, 0.0095 M. The least-squares first-order rate constant of 14 data points was $1.32 \pm 0.01 \times 10^{-4}$ sec^{-1}.

Deuterium Analysis of I by Mass Spectrometry. All quantitative measurements were performed on an AEI MS 9 instrument at 20 ev, 8 accelerating kv, monitor 5–9 $\times$ 50, sample temperature 290°, inlet temperature 230°, source temperature 170°, source slit 30% open, and collector slit 40% open. Data were obtained with potentiometers and a recorder.[31]

(31) Devised by Mr. R. Gillespie.

The following relative intensities were found for I-H, measured (corrected): m/e 252, 0.1842 (0.1915[32]); m/e 251, 1.0000 (1.0000); and m/e 250, 0.207.

The corrected relative intensities were obtained by subtracting 0.207 times the measured 252 intensity from the measured 251 intensity. In subsequent deuterium determinations of mixtures of I-H and I-D, eq 25 and 26 were used to convert observed intensities [$(251)_{obsd}$ and $(252)_{obsd}$] into corrected intensities [$(251)_{cor}$ and $(252)_{cor}$].

$$(252)_{obsd} = (252)_{cor} + 0.191(251)_{cor} \qquad (25)$$

$$(251)_{obsd} = (251)_{cor} + 0.207(252)_{cor} \qquad (26)$$

Because of the complexity of fragmentation, analyses were performed with a calibration curve. Standard mixtures were prepared by weighing amounts of I-H$_\pm$ and I-D$_+$ totalling 100 mg into flasks, dissolving the solids in ether, evaporating the solvent, and thoroughly grinding the recovered solid in a mortar to ensure isotopic homogeneity. Analytical data for the standards are

Table VIII

Known fraction D	$(252)_{obsd}/$ $(251)_{obsd}$	Calcd fraction D	Deviation
0.295	0.556	0.292	−0.003
0.488	0.917	0.473	−0.015
0.681	1.474	0.649	−0.032

reported below. Results were reproducible to ±0.003 atom of D per molecule. A standard containing 0.488 atom of D per molecule was prepared from I-H$_+$ and I-D$_+$. Its analysis was indistinguishable from that reported in the data below, demonstrating that racemate and antipode of I do not fractionate during vaporization into the heated inlet system of the mass spectrometer. All intensity ratios are medians of ratios obtained from three to five separate introductions of the sample into the instrument. Only samples of nearly equal deuterium content were analyzed at one time because amide I had a strong affinity for the walls of the inlet and source of the mass spectrometer, which gave a memory effect. Samples of racemate and antipode from both reresolutions described above and sample J from partial exchange of I-D$_+$ in t-butyl alcohol were analyzed by this procedure. The calculated fraction of deuterium in each unknown sample was corrected by interpolation from the deviations reported for standards (Table VIII).

(32) J. H. Beynon and A. E. Williams, "Mass and Abundance Tables for Use in Mass Spectrometry," Elsevier Publishing Co., New York, N. Y., 1963, report 0.1906 for naturally occurring isotopes in $C_{17}H_{17}NO$.

Studies on Electrolytic Substitution Reactions. III.[1] Isomer Distributions and Isotope Effects in Nuclear and Side-Chain Anodic Acetoxylation of Aromatic Compounds

Lennart Eberson

Contribution from the Department of Chemistry, University of Lund, Lund, Sweden. Received April 27, 1967

Abstract: Using the determination of isomer distributions as an experimental tool, the anodic acetoxylation of representative aromatic compounds in acetic acid–acetate has been investigated with respect to a number of experimental variables, such as the influence of changing the anode potential, the nature of the cation, and the concentration of the acetate ion. As regards the nature of the anion, it has been found that the presence of acetate ion is essential for *nuclear* acetoxylation to occur. A concerted mechanism, involving a two-electron transfer from the π-electron system of the aromatic compound simultaneously with the formation of a C–O bond to an acetate ion, is proposed for this reaction. This type of mechanism is closely similar to that generally assumed to be valid for electrophilic aromatic substitution reactions. Results from isomer distribution studies for anodic nuclear acetoxylation of a number of simple aromatic compounds confirm the validity of this analogy, as do also isotope effect determinations. In sharp contrast to nuclear acetoxylation, it has been found that *side-chain* acetoxylation of alkylaromatic compounds can also be achieved in acetic acid containing salts of other anions, such as perchlorate and tosylate. For side-chain acetoxylation of ethylbenzene an isotope effect $k_H:k_D$ of 2.6 ± 0.3 was determined. The similarity between the product distributions of anodic and manganic acetate acetoxylation of p-methoxytoluene further supports the view that benzyl cations are intermediates in side-chain acetoxylation, although existing data do not allow a differentiation between different mechanisms for their formation.

On the basis of polarographic measurements and preparative electrolyses at controlled anode potential (cpe), it was recently proposed[2] that the anodic acetoxylation of aromatic compounds observed during electrolysis in glacial acetic acid–sodium acetate proceeds *via* an initial two-electron transfer from the π-electron system of the aromatic compound to the anode, followed by a nucleophilic attack of acetate ion on the intermediate dicationic species (eq 1).

$$\mathrm{ArH} \xrightarrow{-2e^-} \mathrm{ArH^{2+}} \xrightarrow{OAc^-} \mathrm{Ar}\!\!\begin{array}{c} H \\ < \\ OAc \end{array} \xrightarrow{-H^+} \mathrm{ArOAc} \qquad (1)$$
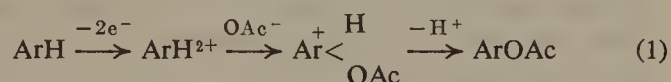
The simultaneously occurring acetoxylation of the α-carbon atom of a side chain of an alkylaromatic compound was accounted for by a similar mechanism,[2] involving an initial two-electron transfer to the anode and loss of a proton to form a benzyl cation which then re-

(1) Part II: L. Eberson and K. Nyberg, *Tetrahedron Letters*, 2389 (1966).
(2) L. Eberson and K. Nyberg, *J. Am. Chem. Soc.*, **88**, 1686 (1966); *Acta Chem. Scand.*, **18**, 1568 (1964).

acts with acetate ion (eq 2). Polar mechanisms have also been invoked to explain the anodic addition of acetoxy groups across double bonds, e.g., in the case of trans-stilbene[3] and cyclooctatetraene.[4]

$$ArCH_3 \xrightarrow{-2e^-} ArCH_3{}^{2+} \xrightarrow{-H^+} ArCH_2{}^+ \xrightarrow{OAc^-} ArCH_2OAc \quad (2)$$
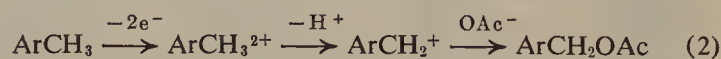
The important feature of these mechanisms is of course the realization of the fact that it is the added aromatic substrate which participates in the primary electrode process and that the acetoxy radical does not play the role of a substituting (or adding) species in these reactions, as has been suggested earlier.[5] In other respects eq 1 and 2 represent simplifications, since they neglect the heterogeneous nature of the process and merely regard the electrode as a source of cationic intermediates. Thus, one cannot ignore the fact that the mechanism should be written as a series of consecutive one-electron transfer steps, as suggested by Perrin[6] (eq 3), or that the acetate ion actually assists in the electron-transfer step[2] (eq 4). In fact, a concerted mechanism involving an acetate ion assisted electron transfer leading

$$ArH \xrightarrow{-e^-} ArH\cdot^+ \xrightarrow{OAc^-} Ar\overset{\overset{\displaystyle H}{|}}{\underset{\displaystyle OAc}{\cdot}} \xrightarrow{-e^-}$$

$$Ar\overset{\overset{\displaystyle H}{|}}{\underset{\displaystyle OAc}{+}} \xrightarrow{-H^+} ArOAc \quad (3)$$

$$(4)$$
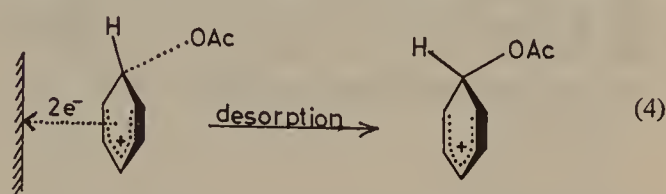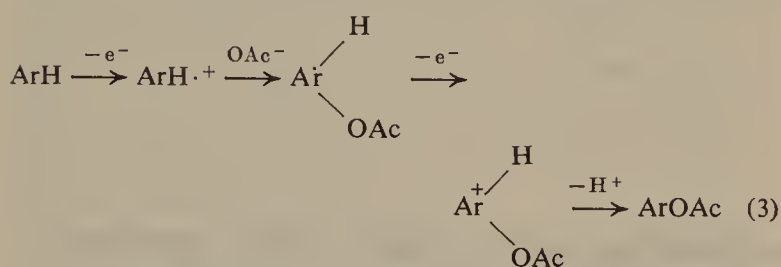
directly to a Wheland-type intermediate (eq 4) would be a close analog to the mechanism of electrophilic aromatic substitution in homogeneous phase.[7]

Likewise, one can describe the side-chain acetoxylation reaction as two consecutive electron transfers (eq 5), a mechanism similar to that proposed by Dewar,

$$ArCH_3 \xrightarrow{-e^-} ArCH_3\cdot^+ \xrightarrow{-H^+} ArCH_2\cdot \xrightarrow{-e^-}$$

$$ArCH_2{}^+ \xrightarrow{OAc^-} ArCH_2OAc \quad (5)$$
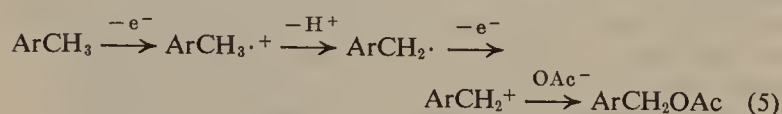
et al.,[8-10] for the oxidation of aromatic compounds by manganic acetate in acetic acid, or as a simultaneously occurring two-electron transfer and cleavage of the α-C–H bond to form a benzyl cation directly (eq 6). In order to attempt to make a differentiation between these

(3) F. D. Mango and W. A. Bonner, J. Org. Chem., 29, 1367 (1964).
(4) L. Eberson, K. Nyberg, M. Finkelstein, R. C. Peterson, S. D. Ross, and J. J. Uebel, J. Org. Chem., 32, 16 (1967).
(5) (a) D. R. Harvey and R. O. C. Norman, J. Chem. Soc., 4860 (1964); (b) C. L. Wilson and W. T. Lippincott, J. Am. Chem. Soc., 78, 4291 (1956); (c) R. P. Linstead, J. C. Bunt, B. C. L. Weedon, and B. R. Shephard, J. Chem. Soc., 3624 (1952).
(6) C. L. Perrin, Progr. Phys. Org. Chem., 3, 165 (1965).
(7) The bookkeeping of electrons in the mechanism of electrophilic aromatic substitution can easily be made to conform to the scheme outlined in eq 4 if the attacking electrophile is allowed to play the electron-accepting role of the anode. Although this procedure is of formal interest only, it is not unreasonable in view of the fact that most electrophiles involved in aromatic substitution must be considered to be very strong oxidants.
(8) P. J. Andrulis, Jr., M. J. S. Dewar, R. Rietz, and R. L. Hunt, J. Am. Chem. Soc., 88, 5473 (1966).
(9) T. Aratani and M. J. S. Dewar, ibid., 88, 5479 (1966).
(10) P. J. Andrulis, Jr., and M. J. S. Dewar, ibid., 88, 5483 (1966).

$$(6)$$

mechanistic alternatives, a study of isomer distributions and isotope effects in the anodic acetoxylation of simple aromatic compounds has been undertaken, and the results of this study are presented in this paper.

Results

Analytical Procedure. In order to determine true isomer ratios in anodic acetoxylation it is of the utmost importance to note that the monoacetates primarily formed are often much less resistant toward oxidation than the starting material, and, besides, that isomeric acetates are oxidized at different rates.[2] Thus, anisole, with a half-wave potential vs. the saturated calomel electrode (sce) of 1.67 v in glacial acetic acid–sodium acetate, is oxidized to a mixture of o-, m-, and p-acetoxyanisole with half-wave potentials of 1.74, 1.25, and 1.12 v, respectively. This means that at a fixed anode potential the meta and para isomers will be consumed preferentially as the electrolysis progresses with a resultant increase in the ortho:para ratio, as indeed preparative runs have shown.[2] To avoid these secondary reactions it is necessary to analyze the product mixture in very early stages of the run. Consequently, samples were withdrawn and analyzed after passage of 1, 2, 3, and 4% of the charge calculated for a two-electron transfer process, and the mean value was then taken to be the isomer distribution. In all cases except one (p-methoxytoluene) no definite trend could be observed during this early period of the reaction, and the average value must therefore represent a close approximation of the true isomer distribution.

After about 10% reaction a gradual change in isomer distribution usually took place, and in cases where half-wave potentials of the isomeric acetates were known,[2] the change was qualitatively in agreement with predictions based on these values. Since previous investigators[5a,11] have analyzed their products after even higher conversions, the preferential oxidation of particular isomer is probably the main reason for the discrepancies between their results and ours (see Table IV).

Influence of the Anode Potential. Next, it was of interest to examine the effect of changing the anode potential upon product distribution. The compounds chosen for investigation differ widely in their susceptibility toward anodic oxidation, as evidenced by the half-wave potentials given in the third column of Table IV. These values are taken from the work of Lund[12] and Neikam, et al.,[13] and have been measured in the system acetonitrile–sodium perchlorate. No attempts were made to determine half-wave potentials in acetic acid–sodium acetate for all the compounds studied, since this electrolyte shows a high background current at potentials above 2 v which would make mea-

(11) S. D. Ross, M. Finkelstein, and R. C. Petersen, ibid., 86, 4139 (1964).
(12) H. Lund, Acta Chem. Scand., 11, 1323 (1957).
(13) W. C. Neikam, G. R. Dimeler, and M. M. Desmond, J. Electrochem. Soc., 111, 1190 (1964).

surements on compounds resistant to oxidation difficult and inaccurate. However, the good linear correlation between the two sets of half-wave potentials observed previously[2] shows that the values measured in acetonitrile reflect the same order of oxidation susceptibility as in acetic acid.

Now, in orientation studies, it becomes necessary to compare product ratios from different reactions run at different anode potentials, and this might be a possible source of systematic error. To examine the magnitude of this effect, anisole was electrolyzed at five different anode potentials in the region 1.2–2.0 v and the product ratio determined. The results, given in Table I, show no significant trend as regards isomer distribution. Naphthalene and ethylbenzene were treated similarly with the same result. Therefore, we feel justified in comparing product ratios obtained at different anode potentials.

Table I. Anodic Acetoxylation of Anisole at Different Anode Potentials[a]

| Anode potential vs. sce, v | Isomer distribution, % | | |
	ortho	meta	para
1.20	68.1	3.7	28.2
1.40	67.4	3.5	29.1
1.60	66.8	3.7	29.5
1.80	67.0	3.3	29.6
2.00	68.3	3.3	28.4

[a] $[OAc^-]$ = 1.00 M, $[PhOCH_3]$ = 0.60 M.

Influence of the Cation. Alkali metal acetates have low dissociation constants[14,15] in acetic acid (of the order of 10^{-7} M) and must therefore exist predominantly as ion pairs under the reaction conditions employed. One might therefore expect that the steric requirements of the ion pair should increase with increasing size of the cation, and that a steric effect should be observable. To test this assumption, t-butylbenzene was electrolyzed in HOAc–MOAc, where M was Li⁺, Na⁺, K⁺, Rb⁺, Cs⁺, and Bu₄N⁺. t-Butylbenzene was chosen in order to have a substituent with large steric requirements of its own, so that any effect of the cation would represent an upper limit. Table II shows that there is a weak trend toward diminishing ortho:para ratios with increasing size of the cation, indicating that it actually may be involved in the process. However, the effect is small and not entirely regular (LiOAc), even in a system where it would be expected to operate at its maximum, so it ap-

Table II. Anodic Acetoxylation of t-Butylbenzene in HOAc–MOAc[a]

| Cation | Isomer distribution, % | | | ortho: para |
	ortho	meta	para	
Li⁺	32.3	21.3	46.4	0.70
Na⁺	35.4	22.1	42.5	0.83
K⁺	33.1	22.0	44.9	0.74
Rb⁺	31.0	22.2	46.8	0.66
Cs⁺	30.1	24.6	45.3	0.66
Bu₄N⁺	28.2	25.0	46.5	0.61

[a] Anode potential 1.90 v vs. sce, [MOAc] = 1.00 M, [Ph-t-Bu] = 0.60 M.

(14) P. J. Proll and L. H. Sutcliffe, *Trans. Faraday Soc.*, **57**, 1078 (1961).
(15) O. W. Kolling and J. L. Lambert, *Inorg. Chem.*, **3**, 202 (1964).

pears safe to conclude that the cation does not play any critical role in determining isomer distribution ratios.

Influence of the Concentration and Nature of the Anion. The variation in the isomer distribution with changes in the sodium acetate concentration is shown for anisole in Table III. On decreasing the acetate ion concentration by a factor of 10, there is a slight decrease in the ortho:para ratio, which may possibly[15] be ascribed to a change in the distribution of species containing acetate ion accompanying changes in [NaOAc].

Table III. Anodic Acetoxylation of Anisole in HOAc–NaOAc[a]

| [NaOAc] | Isomer distribution, % | | |
	ortho	meta	para
1.00	67.4	3.5	29.1
0.33	57.3	3.2	39.5
0.10	60.2	2.2	37.6

[a] Anode potential vs. sce 1.40 v, [PhOMe] = 0.60 M.

Of much more interest is the abrupt change which takes place when acetate ion is replaced by other anions. In this case a fundamental difference between the side-chain and nuclear acetoxylation reactions appears, since *the side-chain reaction does not require the presence of acetate ion in order to occur. In sharp contrast, nuclear acetoxylation cannot be achieved in the absence of acetate ion.* Thus, ethylbenzene gives exclusively the α-acetoxy derivative when electrolyzed in HOAc–NaClO₄ or HOAc–Et₄N⁺OTs⁻, whereas in HOAc–NaOAc the products are partitioned in an approximate 1:1 ratio between the α-acetoxy compound and the three isomeric ethylphenyl acetates (see Table IV). On the other hand, neither anisole nor t-butylbenzene give any trace of nuclear acetoxylation products on electrolysis under those conditions (and also in HOAc–(NH₄)₂SO₄). In these cases, intensely colored solutions were formed, the nature of which have not yet been investigated. Nuclear acetoxylation of anisole could be effected by electrolysis in HOAc–KF, but in this medium species containing acetate ion must be present since fluoride ion is a fairly strong base (the solution had very strong glass-etching properties, indicating the presence of HF).[16]

That acetic acid is not essential as a medium for nuclear acetoxylation is shown by the fact that acetoxyanisoles were formed by electrolyzing anisole in 80% acetonitrile–20% water–(saturated solution) sodium acetate. The ortho:meta:para ratio was 66:5:29, not much different from the results obtained in HOAc–NaOAc (Table I).

The differentiation between nuclear and side-chain acetoxylation now possible is important for preparative applications. Nuclear acetoxylation generally tends to give fairly low yields of monoacetates because of secondary reactions, whereas this problem is not serious for the much more oxidation-resistant side-chain ace-

(16) Dr. S. D. Ross at the Sprague Electric Co., North Adams, Mass., has kindly informed us that he has observed the same differentiation between side-chain and nuclear acetoxylation upon changing the nature of the anion. Toluene undergoes exclusive side-chain acetoxylation in HOAc–NH₄NO₃ with no trace of nuclear acetoxylation product observable. We have restricted ourselves to the use of salts of anions which are oxidized with difficulty, since there is no problem about the nature of the primary electrode process in these cases. Nitrate ion is discharged at much lower anode potentials, and hence radical intermediates must be considered in the discussion of possible mechanisms [cf. S. D. Ross, M. Finkelstein, and R. C. Petersen, *J. Am. Chem. Soc.*, **88**, 4657 (1966)].

Table IV. Isomer Distribution in Anodic Acetoxylation of Aromatic Compounds, [NaOAc] = 1.00 M, [Substrate] = 0.60 M

Compound	Anode potential vs. sce, v	Half-wave potential[a] vs. Ag/Ag+, v	Isomer distribution, %			
			ortho or 1-	meta or 2-	para	α[b]
Toluene[c]	1.90	1.98, 1.93	43.2	11.1	45.7	28.6
Ethylbenzene[d]	1.90	1.96	43.8	10.2	46.0	50.5
Isopropylbenzene	1.90	1.87	44.0	16.5	39.5	46.7
t-Butylbenzene[e]	1.90	1.87	35.4	22.1	42.5	
Diphenylmethane	1.90		42.9	11.8	45.3	18.7
Fluorobenzene	1.96		34.1	8.2	57.7	
Chlorobenzene	2.00	2.07	36.8	5.5	57.7	
Bromobenzene	2.00	1.98	29.8	3.5	66.7	
Iodobenzene[f]	1.75	1.77	17.3	4.3	78.4	
Anisole[g]	1.40	1.35	67.4	3.5	29.1	
Phenyl acetate[h]	1.80		40.1	5.0	54.9	
Biphenyl	1.80	1.48	30.7	0.9	68.4	
Naphthalene[i]	1.70	1.34, 1.31	96.1	3.9		
Benzotrifluoride	2.4	2.6[j]	No acetates formed			
Methyl benzoate	2.4	2.4[j]	No acetates formed			

[a] Data taken from ref 12 and 13. [b] Percentage of total amount of acetoxylation products. [c] Lit.[5a] ortho 47.7, meta 11.2, and para 41.1% at high conversion and non-cpe conditions. [d] Lit.[11] ortho 48, meta 12, para 40, and α 44.5% at high conversion and non-cpe conditions. [e] Lit.[11] ortho 28, meta 27, and para 45% at high conversion and non-cpe conditions. [f] Analyzed after 15–20% conversion. About 90% of product appears as iodoxybenzene. [g] Lit.[5a] ortho 69.9, meta 1.8, and para 28.3% at high conversion and non-cpe conditons. [h] Lit.[11] ortho 56 and para 44% at high conversion and non-cpe conditions. [i] Lit.[11] 1- 84 and 2- 16% at high conversion and non-cpe conditions. [j] Estimated value.

toxylation products. The possibility of obtaining the side-chain acetoxylation product exclusively in media as HOAc–NaClO$_4$ or HOAc–Et$_4$+ OTs$^-$ would therefore be synthetically valuable.

Isomer Distribution Studies. Having established that the anode potential, the nature of the cation, and the concentration of acetate ion influence the isomer distribution in representative systems to a small extent only, the reaction conditions for a systematic study of isomer distributions could be fixed to the use of glacial acetic acid 1.00 M in sodium acetate and 0.60 M in substrate. If possible, the anode potential was kept at a value lower than the half-wave potentials given in Table IV in order to keep it lower than the critical potential for discharge of acetate ion. The temperature of the electrolyte was kept at 30°.

Following the analytical procedure described above, the isomer distributions shown in Table IV were obtained. It should be noted that the percentage of side-chain acetoxylation product is based on the total amount of products, whereas the figures for the ortho, meta, and para isomer of an alkylaromatic compound are based on the amount of nuclear acetoxylation products only in order to facilitate comparisons with other data.

In one case, iodobenzene, the reaction had to be run to an extent of 15–20% before acetoxylation products sufficient for satisfactory analyses had accumulated. This is due to the factor that the major pathway for anodic oxidation of iodobenzene gives rise to products in which the oxidation state of the iodine atom has changed. In this particular case iodoxybenzene could be identified among the products (no doubt small amounts of iodosobenzene and/or its diacetate were also formed), as has been found also in the electrolysis of iodobenzene in aqueous acetic acid.[17] Recent studies by Miller and Hoffman[18] have demonstrated that a similar reaction is predominant in cpe of iodobenzene in acetonitrile–lithium perchlorate, leading to 4-iodophenyliodonium perchlorate.

In good agreement with the postulate that the primary electrode process is an electron transfer from the aromatic compound to the anode, benzene derivatives containing strongly electron-withdrawing substituents (CF$_3$, COOMe) do not undergo acetoxylation under the conditions employed. Such substituents lower the energy of the highest filled π orbital of the molecule and hence it is more difficult to remove electrons from this orbital. From the excellent correlation between half-wave potentials in acetonitrile–sodium perchlorate and photoionization potentials,[13] it can be estimated from the photoionization potential of benzotrifluoride[19] (9.68 ev) that its half-wave potential in this medium would be about 2.6 v and hence about 2.9 v in HOAc–NaOAc vs. sce.[2] The photoionization potential of methyl benzoate does not appear to be known, but the value for benzaldehyde (9.51) gives 2.7 v as a crude estimate of the half-wave potential in HOAc–NaOAc. Thus, before one can attain an anode potential high enough for oxidizing these compounds, discharge of acetate ion will take place and be the predominant electrode reaction. This constitutes another piece of evidence speaking strongly against the intervention of acetoxy radicals as substituting species in anodic acetoxylation, since aromatic compounds with strongly electron-withdrawing substituents are actually very good substrates in homolytic substitution processes, e.g., in homolytic hydroxylation by Fenton's reagent[20] or H$_2$O$_2$–Fe^{III}–catechol.[21] The situation is similar in homolytic alkylation and arylation processes,[20,22] and also in cases where the substituting radicals are produced anodically.[23]

Isotope Effects. To see if a primary deuterium isotope effect could be observed in side-chain acetoxylation, a preparative electrolysis of ethylbenzene-α-d in

(17) F. Fichter and P. Lotter, *Helv. Chim. Acta*, **8**, 438 (1925).
(18) L. L. Miller and A. K. Hoffman, *J. Am. Chem. Soc.*, **89**, 593 (1967).

(19) D. W. Turner, *Advan. Phys. Org. Chem.*, **4**, 31 (1966).
(20) G. H. Williams, "Homolytic Aromatic Substitution," Pergamon Press Inc., New York, N. Y., 1960, p 110 ff; R. O. C. Norman and G. K. Radda, *Proc. Chem. Soc.*, 138 (1962).
(21) G. A. Hamilton, J. W. Hanifin, Jr., and J. P. Friedman, *J. Am. Chem. Soc.*, **88**, 5269 (1966).
(22) J. R. Shelton and C. W. Uzelmeier, *ibid.*, **88**, 5222 (1966).
(23) For a summary, see L. Eberson in "Chemistry of the Carboxyl Group," S. Patai, Ed., Interscience Publishers, Inc., London, in press.

Table V. Anodic Acetoxylation of Ethylbenzene-α-d^a

Compound	Isomer distribution, % of total products			
	ortho	meta	para	α
Ethylbenzene	21.5	5.1	23.5	49.9
Ethylbenzene-α-d	25.4	5.9	26.2	42.5

^{a} Anode potential 2.00 v vs. sce, [NaOAc] = 1.00 M.

Table VI. Anodic Acetoxylation of Deuterated Anisoles^a

Compd	Isomer distribution, %		
	ortho	meta	para
Anisole	67.4	3.5	29.1
Anisole-o-d	67.3	3.0	29.7
Anisole-p-d	64.9	4.2	30.9

^{a} [NaOAc] = 1.00 M, anode potential 1.40 v vs. sce.

The products isolated from manganic acetate oxidation of PMT in HOAc at 70° (molar ratio of oxidant to PMT = 1:1) were recovered PMT (54.1%), p-methoxybenzyl acetate (40.5%), 2- and 3-acetoxy-4-methylanisole (yield not specified but claimed to be small), p-methoxybenzaldehyde (4.6%), and 1,2-bis(p-methoxyphenyl)ethane (yield not specified but claimed to be small).[8] Kinetic studies, mainly concerned with the determination of "initial rates" of disappearance of manganic acetate (during the first 10% of the reaction), made probable a mechanism of the electron-transfer type (eq 7).[8]

$$ArCH_3 + Mn(OAc)_3 \rightleftharpoons (ArCH_3^+), OAc^- + Mn(OAc)_2$$
intimate ion pair

$$[(ArCH_3^+), OAc^-] \longrightarrow ArCH_2\cdot + AcOH$$

$$ArCH_2\cdot + Mn^{III} \longrightarrow ArCH_2^+ + Mn^{II}$$

$$ArCH_2^+ + AcOH \longrightarrow ArCH_2OAc + H^+ \qquad (7)$$

Table VII. Manganic Acetate Oxidation of PMT in Glacial HOAc at 70°^{a}

Time, hr	Total yield of products, %	Product distribution, mole %			Ratio aldehyde/ acetate
		p-Methoxy-benzaldehyde	p-Methoxy-benzyl acetate	2-Acetoxy-4-methylanisole	
0.5	1.8	40	60	<0.1	0.67
1	2.8	34	66	<0.1	0.51
2	4.9	30	70	<0.1	0.43
5	8.3	25	75	<0.1	0.33
25	19.0	13	87	<0.1	0.15
52	31	9	91	<0.1	0.10
80	36	10	90	<0.1	0.11
∞	46	9^b	91	<0.1	0.10
∞	47	10^c	90	Not reported	0.11

^{a} [PMT] = [Mn(OAc)$_3$·2H$_2$O] = 0.125 M. ^{b} Nmr analysis on the crude mixture gave an aldehyde/acetate ratio of 12:88. ^{c} Data from ref 8.

HOAc–NaOAc was performed. After hydrolysis, 1-phenylethanol was isolated and the percentage of deuterium label in the α position was determined (by nmr) to be 65 ± 2%, corresponding to a $k_H:k_D$ ratio of 2.6 ± 0.3. A similar but less accurate figure, 2.3 ± 0.7, could be calculated from the change in isomer distribution observed in the acetoxylation of ethylbenzene and ethylbenzene-α-d, respectively (Table V). Thus, C–H bond loosening is implied in the transition state of the rate-determining reaction, which is similar to what is observed[8] in the homogeneous side-chain acetoxylation of the methyl group of p-methoxytoluene by manganic acetate in glacial acetic acid, postulated to occur via an electron-transfer mechanism of the same type as that depicted in eq 5 (see eq 7 below). In this case the $k_H:k_D$ ratio was about 5, although for reasons discussed below this value may not be correct.

To study the effect of deuterium substitution in nuclear acetoxylation, o- or p-deuterioanisole was electrolyzed in HOAc–NaOAc and the isomer distribution determined. The mean value from several runs gave small deviations from the isomer ratio obtained with the protio compound, but the calculated isotope effects, $(k_H/k_D)_p$ = 0.9 ± 0.1 and $(k_H/k_D)_o$ = 1.0 ± 0.1, are hardly significantly different from unity (see Table VI).

Anodic vs. Manganic Acetic Oxidation of p-Methoxytoluene. The publication of a series of papers on aromatic oxidation by electron transfer[8–10] immediately suggested a comparison between anodic and manganic acetate acetoxylation of p-methoxytoluene (PMT) in order to see if there are any differences with regard to product distribution between these processes.

However, following our practice of analyzing the product at early stages of the run in order to minimize secondary reactions, quite different product distributions were observed. Specifically, it was hoped that the formation of p-methoxybenzaldehyde, assumed[8] to be formed via further oxidation of p-methoxybenzyl acetate to the aldehyde diacetate (which analyzes as the aldehyde on vpc), would be suppressed during the first few per cent of the reaction. Contrary to expectations, an initially high aldehyde to acetate ratio was observed, and this ratio then slowly decreased to a final value close to that reported previously[8] (see Table VII). Nmr analysis of the crude product mixture demonstrated that the aldehyde was formed as such and not as its diacetate.

Since manganic acetate contains two molecules of crystal water it seemed reasonable to assume that water, possibly preferentially bound to the manganic ion, partially replaces acetate ion as a nucleophile during the early phases of the reaction, resulting in the formation of p-methoxybenzyl alcohol. This is known[8] to be oxidized by manganic acetate at approximately the same rate as the starting material (relative alcohol:PMT = 0.95:1). p-Methoxybenzyl acetate cannot possibly be the precursor of the aldehyde, since the diacetate is not formed and the ratio between the oxidation rates of PMT and the acetate is 1:0.035, far too high to account for more than a small proportion of the aldehyde actually formed.

To study the possible role of water during the early stages of the reaction, it was run with 2.5% of water added (Table VIII) and in a medium consisting of

Table VIII. Manganic Acetate Oxidation of PMT in Wet[a] Acetic Acid at 70°[b]

| Time, hr | Product distribution, mole % | | | |
	p-Methoxy-benz-aldehyde	p-Methoxy-benzyl acetate	2-Acetoxy-4-methyl-anisole	Ratio aldehyde/acetate
0.5	58	42	<0.1	1.38
1	48	52	<0.1	0.92
2	40	60	<0.1	0.67
5	24	76	<0.1	0.32
25	13	87	<0.1	0.15
∞	10	90	<0.1	0.11

[a] 2.5% water added. [b] [PMT] = [Mn(OAc)₃·2H₂O] = 0.125 M.

Table IX. Manganic Acetate Oxidation of PMT in Preconditioned[a] Medium at 70°[b]

| Time, hr | Product distribution, mole % | | | |
	p-Methoxy-benz-aldehyde	p-Methoxy-benzyl acetate	2-Acetoxy-4-methyl-anisole	Ratio aldehyde/acetate
0.5	4.8	95.2	<0.1	0.051
1	3.1	96.9	<0.1	0.032
2	1.7	98.3	<0.1	0.017
5	1.1	98.9	<0.1	0.011
25	1.4	98.6	<0.1	0.014
∞ [c]	1.5	98.3	0.20	0.015

[a] Mn(OAc)₃·2H₂O was added to HOAc containing 4% of acetic anhydride and kept at 70° for 20 hr. Shorter preconditioning periods resulted in higher aldehyde/acetate ratios. [b] [PMT] = [Mn(OAc)₃·2H₂O] = 0.125 M. [c] The product distribution is calculated only on the basis of the products mentioned in the table. Two unknown compounds, each having a molecular ion mass number of 194, were also visible in the gas chromatograms. These comprised 15.8 and 2.6%, respectively, of the *total* product mixture.

Table X. Anodic *vs*. Manganic Acetate Oxidation in PMT

| Oxidant, medium | Amount of charge, % of theoret | Product distribution, mole % | | | |
		p-Methoxy-benzaldehyde	p-Methoxy-benzyl acetate	2-Acetoxy-4-methylanisole	3-Acetoxy-4-methylanisole
Anodic oxidation in HOAc, preconditioned with acetic anhydride, at 30°	1.5	7.8	89.5	2.7	0.1
	2.5	6.6	91.3	2.0	0.07
	3.8	3.9	92.4	3.5	0.2
	7.5	3.4	93.1	3.4	0.1
	14	3.5	91.0	4.9	0.6
	40	11.4	83.8	4.3	0.5
Anodic oxidation in HOAc, preconditioned with acetic anhydride, at 70°	2.5	5.7	93.4	0.85	0.05
	5.0	3.6	95.4	0.9	0.1
	9.0	3.5	95.2	1.1	0.2
Mn(OAc)₃ oxidation in HOAc, preconditioned with Ac₂O, at 70°	3[a]	1.7	98.3	<0.1	
	5[a]	1.1	98.9	<0.1	

[a] Estimated per cent conversion.

Mn(OAc)₃·2H₂O in glacial acetic acid, preconditioned with 5% of added acetic anhydride for 20 hr at 70° before the addition of PMT (Table IX). The drastic effect on the aldehyde to p-methoxybenzyl acetate ratio clearly demonstrates that the water content of manganic acetate creates a different situation during the first 10–20% of the reaction as compared to the anhydrous case. Fortunately, p-methoxybenzyl alcohol is oxidized at nearly the same rate as PMT, so conclusions based on initial rate measurements are probably not much affected. On the other hand, oxidation rates are not known for PMT-α,α,α-d₃ and p-methoxybenzyl alcohol-

α,α-d₂, so that the isotope effect reported[8] may be in error.

Having identified this source of error, comparisons between anodic and manganic acetate oxidation of PMT were based on runs in media which had been preconditioned by a small amount of acetic anhydride. The results are shown in Table X. Two products, not previously observed and as yet unidentified, both having a molecular ion peak at mass number 194 (corresponding to p-methoxybenzyl acetate + a methylene group), were found in the final product mixture from manganic acetate oxidation of PMT. It appears reasonable to assume that the slow spontaneous decomposition[9] of manganic acetate is responsible for the formation of these compounds. In a manner similar to the cobaltic ion oxidation of acetate ion[24] this reaction would produce methyl radicals which would then have a chance to be captured by PMT and/or its acetoxylation products. Lead tetraacetate oxidations of aromatic compounds are complicated by the same type of reaction.[5a,25]

Even if care has been taken to remove water as completely as possible from the media used there is still a trend toward initially high aldehyde to acetate ratios both in the anodic and manganic acetate case (Tables IX and X). Autoxidation of an intermediate benzyl radical is a possible explanation for this effect, since no special precautions were taken to remove oxygen completely from the solutions.

If the comparison between the two types of oxidations is restricted to an interval where the aldehyde percentage has assumed a steady value (*i.e.*, in the range of 5–10% reaction), one notes that the product distributions are closely similar, except possibly for the fact that nuclear acetoxylation occurs to a larger extent in the anodic case. Another noticeable feature of Table X is the temperature effect on the anodic process, the proportion of side-chain acetoxylation product increasing with temperature.

Discussion

Nuclear Acetoxylation. Our previous suggestion[2] that the anodic acetoxylation of an aromatic nucleus should be described by the mechanism depicted in

(24) A. A. Clifford and W. A. Waters, *J. Chem. Soc.*, 2796 (1965).
(25) R. Criegee in "Oxidation in Organic Chemistry," Part A, K. B. Wiberg, Ed., Academic Press Inc., New York, N. Y., 1965 p 277.

eq 1 (or eq 3, as preferred by Perrin[6]) was mainly intended to emphasize that electron transfer from the aromatic compound to the anode is the primary electrochemical step. The possibility that the nucleophile might actually assist in the electron-transfer step was discussed and by no means ruled out, but at that time existing data did not allow a decision between these alternatives. Some indications that one-electron transfers are favored in very weakly nucleophilic media and that nucleophile-assisted two-electron transfers are favored in more nucleophilic media were indeed to be found,[2] but these results did not easily lend themselves to an extrapolation to the behavior of the acetic acid–acetate system.

The finding that the presence of acetate ion is essential for the occurrence of nuclear acetoxylation and that the isomer distribution in anodic acetoxylation of anisole is somewhat dependent on the acetate ion concentration (Table III) strongly supports the view that acetate ion or an acetate–metal ion pair assists the electron-transfer step. Since the alkali metal acetates (and probably also $Bu_4N^+OAc^-$ [26]) have dissociation constants of the order of 10^{-7} M in HOAc, the predominant acetate ion containing species must be the ion pair. This would therefore likely be the active species, although one cannot exclude the fact that the field gradient near the anode forces a separation of the two ions. The weak steric effect of the cation (Table II) would seem to favor the ion pair as the active species, although opinion must be reserved at this point since the dissociation constants of different alkali metal acetates exhibit slight differences. An additional source of uncertainty is that data from different investigations disagree to a certain extent,[15,16] and hence a more detailed treatment must await further experimentation. The important conclusion that acetate ion in some form is involved in the product-determining step is not affected by these marginal problems.

Thus, the first refinement of eq 1 would be to include acetate ion in the product-determining step. Equation 8 is an attempt to do this. It consists of an adsorption
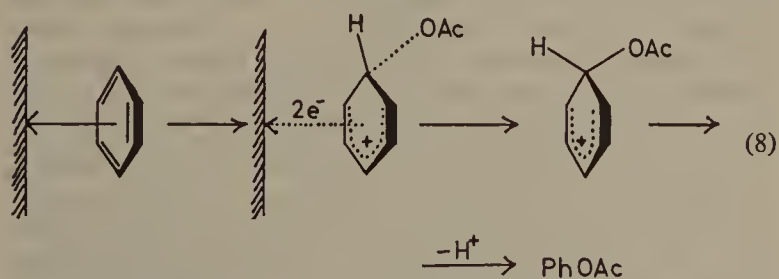
step in which the aromatic compound is adsorbed to the anode, most likely *via* its π-electron system. In the second and rate-determining step, two electrons are transferred to the anode simultaneously with the formation of a carbon to oxygen bond to an acetate ion, resulting in the formation of a Wheland-type intermediate which is desorbed from the anode and gives product by loss of a proton.

Equation 8 represents a mechanism entirely analogous to that generally assumed to be valid for electrophilic aromatic substitution in homogeneous phase (π-complex formation between substrate and electrophile, a rate-determining attack of the electrophile on one of the

ring carbons, formation of a Wheland intermediate, followed by rapid proton loss). If one postulates this kind of mechanism, one would expect that anodic acetoxylation would show the general characteristics of electrophilic aromatic substitution reactions, with regard to both isomer distribution and isotope effects.

The results shown in Table IV do indeed demonstrate a close resemblance between anodic acetoxylation and electrophilic aromatic substitution. Although the data cannot be treated quantitatively according to the Brown–Stock selectivity treatment[27] because of the lack of suitable data correlating relative rates of the substrates used, the fairly high proportion of *meta* derivatives observed in most cases (anisole, alkyl- and halobenzenes) suggests that the system anode–acetate should preferably be described as a low-selectivity "reagent." Some ambiguity is attached to this conclusion, though, since the result for biphenyl does not fit in very well.

A weak steric effect is indicated by the decreasing *ortho*:*para* ratios in the halobenzene series and for the pair isopropylbenzene–*t*-butylbenzene.

The absence of a significant positive deuterium effect on the *ortho* and *para* acetoxylation of anisole is another important similarity with electrophilic substitution reactions of this compound[28] (Table VI).

We do not think it worthwhile to discuss the orientation data and isotope effects in more detail at present, since too far reaching comparisons with homogeneous processes might lead to faulty conclusions. We are forced to conclude, however, that anodic acetoxylation has many of the characteristic features of an electrophilic aromatic substitution reaction, and therefore that the mechanism given in eq 8 should provide the best picture of nuclear anodic acetoxylation.

Side-Chain Acetoxylation. Equation 2 shows the mechanism previously suggested for side-chain acetoxylation.[2] The formation of a benzyl cation *via* an initial two-electron transfer from the alkylaromatic compound to the anode and subsequent loss of a proton from an α carbon are clearly the most important features of this mechanism. It has now been established that the presence of acetate ion is not a necessary requirement for side-chain acetoxylation to occur, and that acetic acid containing salts of different electrochemically inert anions (ClO_4^-, OTs^-, SO_4^{2-}) is just as good or even better as a medium. Moreover, alkylbenzenes have been shown to undergo anodic side-chain acetamidation on electrolysis in acetonitrile–sodium perchlorate[1] which is very difficult to rationalize if the intermediacy of benzyl cations is not postulated.

Accordingly, a benzyl cation is the most probable intermediate in side-chain acetoxylation, even if the mechanism in eq 2 must be slightly modified to accommodate the isotope effect observed. This was found to be 2.6 ± 0.3, implying a certain amount of C–H bond breaking in the transition state of the rate-determining step. This means that a concerted mechanism (eq 6), a rate-determining proton loss from the dication of eq 2, or a rate-determining proton loss from the cation radical of eq 5 must be considered. Existing data do not allow a differentiation between these alternatives, although the close similarity between anodic and

(26) *Cf.* E. Grunwald and E. Price, *J. Am. Chem. Soc.*, 86, 2956 (1964).

(27) L. M. Stock and H. C. Brown, *Advan. Phys. Org. Chem.*, 1, 35 (1963).

(28) For a review, see H. Zollinger, *ibid.*, 2, 163 (1964).

Table XI. Vpc Conditions for Analysis of Acetate Mixtures

Compound	Column[a]	Temp, °C	ortho or 1-	meta or 2-	para	α
				Retention time of acetate, min[b]		
Toluene	A[c]	120	18.0	25.0	23.2	7.4
Ethylbenzene	B	120	10.3	13.0	14.0	8.4
Isopropylbenzene	B	110	15.8	21.2	24.2	12.2
t-Butylbenzene	C	120	22.8	25.4	32.0	
Diphenylmethane	B	180	16.4	24.0	27.0	13.0
Fluorobenzene	D	80	71.4	78.0	82.0	
Chlorobenzene	B	120	13.2	15.6	16.6	
Bromobenzene	B	130	14.9	18.4	19.6	
Iodobenzene	E	140	43.4	54.4	57.8	
Anisole	B	130	13.1	17.9	19.6	
Phenyl acetate	F	150	30.0	41.0	43.4	
Biphenyl	B	180	9.4	23.6	26.4	
Naphthalene	C	180	15.0	16.8		

[a] Column A, 2 m × 0.3 cm 10% trixylenyl phosphate on Chromosorb W 80–100; B, 2 m × 0.3 cm 5% neopentyl glycol succinate on Chromosorb P 80–100; C, 2 m × 0.3 cm 10% Apiezon L on Chromosorb P 80–100; D, same as C but 4 m in length; E, 2 m × 0.3 cm 10% butanediol succinate polyester on Chromosorb W 80–100 in combination with column B; F, same as B but 4 m in length. [b] Nitrogen flow rate 30 cc/min. [c] Analyzed as a mixture of cresols and benzyl alcohol.

manganic acetate acetoxylation (Table X) of PMT would seem to favor the last-mentioned one.

Concluding, we wish to emphasize that anodic acetoxylation can be described mechanistically in very much the same way as similar homogeneous processes of the electrophilic type. Differences which can be traced back to the heterogeneous nature of the electrolytic reaction have not yet been found. It is hoped that stereochemical studies of the side-chain acetoxylation reaction will provide some insight into this complex problem.

Experimental Section

Materials. Analytical grade acetic acid was distilled through a ten-plate column before use, a middle fraction comprising about 70% of the batch being collected. Analytical grade inorganic reagents were used throughout for preparing the electrolytes. Manganic acetate was prepared according to the method given by Dewar, et al.[8]

The organic compounds studied were purchased in the purest quality available and carefully checked for impurities by vpc. If the region in which the corresponding monoacetates eluted was not entirely clean at high attenuations, the compound was further purified by distillation or preparative vpc. For use as reference compounds, all the monoacetates of the compounds listed in the first column of Table IV (except benzotrifluoride, in which case only the m-acetate was prepared) were synthesized from commercially available phenols according to well-known procedures. 4-Methoxybenzylidene diacetate and 2- and 3-acetoxy-4-methylanisole were prepared according to the methods given by Dewar, et al.[8] The deuterium-labeled compounds were synthesized by treating the appropriate Grignard reagent with D_2O.

Procedure. The isomer distribution experiments were carried out using the same electrolysis cell set-up as that described earlier,[2] except that the volume of the vessel was 60 ml. The appropriate electrolyte (50.0 ml, 0.6 M in substrate and 1.00 M in supporting electrolyte in the case of the acetates, unless otherwise required, and saturated with respect to other supporting electrolytes referred to above) was poured into the cell and allowed to reach thermal equilibrium (30°). The anode potential was controlled by means of a Model 557 potentiostat from Amel, Milan, Italy, and the charge passed through the electrolyte was measured by means of the Model 558 integrator from the same company. After starting the electrolysis, 2.00-ml samples were withdrawn after passage of 1, 2, 3, and 4% of the theoretically calculated amount of charge (except in the case of iodobenzene, as mentioned above). Each sample was worked up by pouring it into saturated bicarbonate solution (20 ml), extracting the organic components with analytical grade ether, and washing the ether extracts with saturated bicarbonate solution. Finally, the ether solution was concentrated to a volume of about 0.4 ml, and the products were analyzed by

vpc (Perkin-Elmer 880 gas chromatograph, equipped with a disk integrator) under the conditions given in Table XI. Adequate checks on the work-up procedure using acetic acid solutions of known composition were made. It is estimated that the percentages given are correct to ±0.5% (absolute value).

In cases where monoacetates have not been isolated and identified previously,[2,11] identification was based on vpc comparisons with authentic samples at several temperatures on several columns. Mass spectrometry was also used for identification in some cases (LKB A-9000 mass spectrometer, equipped with a gas chromatography inlet).

Anodic Oxidation of Iodobenzene. Iodobenzene (0.15 mole) in 250 ml of acetic acid–sodium acetate (1.00 M) was electrolyzed at an anode potential of 1.80 v vs. sce until 9000 coulombs had passed through the electrolyte. The solution was then dropped into a vigorously stirred slurry of sodium bicarbonate (320 g) in water (700 ml). One extraction with ether removed ether-soluble organic materials, and then the aqueous layer was allowed to stand for 1 week. A small amount of a solid (0.9 g) was collected by filtration. A sample was recrystallized from water; explosion point of the pure product was about 240°, infrared spectrum identical with that of authentic iodoxybenzene.

Anodic Oxidation of Ethylbenzene-α-d. Ethylbenzene-α-d (0.15 mole, containing 7 ± 0.5% of protio compound according to nmr analysis) in 250 ml of acetic acid–sodium acetate (1.00 M) was electrolyzed at an anode potential of 2.00 v vs. sce until vpc analysis of a small sample indicated a 35–40% conversion into acetates. The solution was dropped into a vigorously stirred slurry of sodium bicarbonate (320 g) in water (700 ml). The organic product was taken up in ether (three 100-ml portions) and then the ether evaporated in vacuo. The residue was treated with a solution of potassium hydroxide (3.5 g), ethanol (60 ml), and water (20 ml) overnight at room temperature. After distilling off most of the ethanol in vacuo, water was added, and the organic products were taken up in ether. The cresols were removed by washing with 0.1 M potassium hydroxide (three 50-ml portions) and water (20 ml). After drying with anhydrous magnesium sulfate, distillation gave 1-phenylethanol (1.2 g), bp 50–51° (0.3 mm). Nmr analysis of this product gave the percentage of 1-phenylethanol-1-d as 65 ± 1% (integration of all signals) and 64 ± 1% (integration of methyl group signal only).

Anodic Oxidation of PMT. The medium used for anodic oxidation of PMT was made by adding 2% acetic anhydride to acetic acid–sodium acetate solution and refluxing the solution overnight.

Manganic Acetate Oxidations. These were performed in stoppered flasks (100-ml volume), containing 80-ml samples 0.125 M in $Mn(OAc)_3 \cdot 2H_2O$ and 0.125 M in PMT with glacial acetic acid (Table VII) or glacial acetic acid containing 2.5% of water (Table VIII) as solvent. In the third case (Table IX) the manganic acetate solution was first made 5% with respect to acetic anhydride and kept at 70° for 20 hr before addition of PMT. Samples were withdrawn at suitable intervals, worked up, and analyzed as described above. Vpc was carried out using column B (see Table XI). At a column temperature of 130° and a nitrogen flow rate of 30 cc/min, retention times (minutes) of products were: p-methoxy-

benzaldehyde, 14.6; 2-acetoxy-4-methylanisole, 16.8; 3-acetoxy-4-methylanisole, 20.0; p-methoxybenzyl acetate, 28.0; unknown peak I (molecular weight 194), 30.5; and unknown peak II (molecular weight 194), 38.2.

The Transition State for Base-Catalyzed Cleavage of the Silicon–Oxygen Bond[1]

Richard L. Schowen and Kenyon S. Latham, Jr.

Contribution from the Department of Chemistry, University of Kansas, Lawrence, Kansas 66044. Received March 20, 1967

Abstract: Substituent correlations and solvent isotope effects have been examined for the general base catalyzed methanolysis of aryloxytriphenylsilanes, previously shown to follow a protolytic mechanism. The solvent isotope effects for p-chlorophenoxytriphenylsilane are $k_H/k_D = 1.25 \pm 0.06$ (acetate ion catalysis) and 1.35 ± 0.06 (methoxide ion catalysis), consistent with "solvation-rule" behavior. Curvature in the free-energy relations for leaving-group structural variation is analyzed and is tentatively interpreted in terms of π bonding of the leaving group to silicon in the activated complex or of a change in mechanism with substituent.

Our earlier observation[1] that the methanolysis of phenoxytriphenylsilane is subject to general base catalysis by phenoxide ion, leading to the conclusion that the reaction follows a protolytic pathway (eq 1), further substantiates a general resemblance of these reactions to the cleavage of carboxylic and phosphate esters. We have therefore undertaken a more detailed characterization of the transition state for base-catalyzed solvolysis of silicon–oxygen compounds, by use of isotope and substituent effects.

$$B + CH_3OH + R_3SiOAr \longrightarrow$$

$$\left[CH_3O \cdots \underset{\underset{HB}{\vdots}}{\overset{|}{Si}} \cdots OAr \text{ or } CH_3O \cdots \underset{\underset{HB}{\vdots}}{\overset{|}{Si}} \cdots OAr \right] \longrightarrow \text{products} \quad (1)$$

$$\text{I} \qquad\qquad \text{II}$$
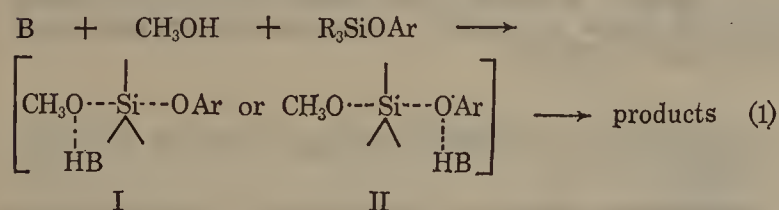
Results

Observed rate constants for methanolysis of five aryloxytriphenylsilanes in acetic acid–acetate ion buffers in methanol and methanol-d_1 (CH$_3$OD) and in phenol–phenoxide ion buffers in methanol are given in Table I. The results may be summarized by the kinetic law of eq 2, where S represents the substrate organosilicon compound and the summation is over all bases, B_i, in the solution. The values of the catalytic constants of eq 2 are shown in Table II. From corresponding rate constants in methanol and methanol-d, the isotope effects for methanolysis of p-chlorophenoxytriphenylsilane, catalyzed by acetate and methoxide ions, can be calculated.

$$(k_H/k_D)_{CH_2CO_2^-} = 1.25 \pm 0.06$$

$$(k_H/k_D)_{CH_3O^-} = 1.35 \pm 0.06$$

$$v = [S]\left\{ k_0 + \sum_i k_i[B_i] \right\} \quad (2)$$

Discussion

Solvent Isotope Effects. The activated complex drawn in eq 1 for the reaction under study depicts a proton undergoing transfer from or to the catalyst. If such a transfer were part of the primary activation process, so that the proton would be in an unstable potential at the activated complex, a primary isotope effect of about 7.8, corresponding to the Brønsted β value[1] of about 0.7, would have been expected.[2] The observed isotope effects are much smaller than the predicted ones, and it therefore appears likely that the proton is not in an unstable potential at the activated complex; the BH moiety is presumably stabilizing the activated complex by a hydrogen-bonding interaction, as postulated by Swain and his co-workers[3] for other examples of general catalysis in protic solvents. The methanolysis of aryloxysilanes appears to conform to the "solvation rule" classification[3] as do carbonyl derivative reactions in which the leaving group is an oxyanion.[2]

These isotope effects present an interesting contrast to the striking observation of Menger[4] that methoxide ion attack on p-nitrophenyl acetate proceeds 2.6 times more rapidly in methanol-d than in methanol at $-78°$. If a completely exponential temperature dependence with unit preexponential factor is assumed ($k_H/k_D = \exp(-a/T)$) the inverse isotope effect is still 1.9 at 25°, equal to the effect reported by Menger[4] for methoxide attack on phenyl benzoate at 25°. The regular effects

(1) Catalysis in Organosilicon Chemistry. II. For part I, see R. L. Schowen and K. S. Latham, Jr., *J. Am. Chem. Soc.*, **88**, 3795 (1966). For further details, see K. S. Latham, Jr., Ph.D. Thesis, University of Kansas, Oct 1966. This work was supported by the National Science Foundation under Research Grant No. GP 3539 and by the National Institutes of Health under Research Grant No. GM 12477-02 and was carried out in part at the Computation Center of the University of Kansas.

(2) The primary isotope effect prediction is made with the aid of Figure 1 of R. L. Schowen, H. Jayaraman, L. Kershner, and G. W. Zuorick, *J. Am. Chem. Soc.*, **88**, 4008 (1966).

(3) C. G. Swain, D. A. Kuhn, and R. L. Schowen, *ibid.*, **87**, 1553 (1965).

(4) F. M. Menger, *ibid.*, **88**, 5356 (1966).

Table I.[a] Observed Rate Constants for Methanolysis of $XC_6H_4OSi(C_6H_5)_3$ in Methanolic Buffer Solutions at $27.4 \pm 0.1°$

X	[B]/[BH]	[B], M	$10^3 k_{obsd}$[b]	X	[B]/[BH]	[B], M	$10^3 k_{obsd}$[b]
Acetate–Acetic Acid Buffers, Methanol-h					5.0	0.0375	5.69
					5.0	0.0750	7.33
p-CH₃O	15.0	0.0750	1.80		5.0	0.1125	8.87
	15.0	0.1150	1.81	m-CF₃	4.76	0.0500	47.2
	15.0	0.1500	1.94		4.76	0.0750	63.2
	12.0	0.1200	1.61		4.76	0.1000	73.4
	10.7	0.0300	1.23		3.46	0.0500	38.9
	10.7	0.0600	1.26		3.46	0.0750	52.5
	10.7	0.0900	1.34		3.46	0.1000	66.3
	10.7	0.1200	1.40		2.68	0.0500	33.3
	10.0	0.0500	1.18		2.68	0.0750	48.2
	10.0	0.1000	1.20		2.68	0.1000	61.2
	10.0	0.1500	1.30	Phenoxide–Phenol Buffers, Methanol-h			
	5.0	0.0500	0.69				
	5.0	0.0600	0.77	p-CH₃O	0.100	0.0005	21.2[b]
	5.0	0.0900	0.83		0.100	0.0010	19.2
	5.0	0.1200	0.84		0.100	0.0015	26.2
					0.050	0.0005	6.11
p-CH₃	15.0	0.0500	1.80		0.050	0.0010	7.63
	15.0	0.1000	1.83		0.050	0.0015	8.06
	15.0	0.1500	1.98				
	10.0	0.0500	1.34	p-CH₃	0.050	0.0005	5.39
	10.0	0.1000	1.44		0.050	0.0010	6.09
	10.0	0.1500	1.53		0.050	0.0015	6.51
	5.0	0.0500	0.71				
	5.0	0.1000	0.83	H	0.050	0.0005	10.0
	5.0	0.1500	0.88		0.050	0.0010	11.2
					0.050	0.0020	15.5
H	15.0	0.0500	2.88	p-Cl	0.050	0.0001	21.6
	15.0	0.1000	3.18		0.050	0.0003	34.3
	15.0	0.1500	3.37		0.050	0.0005	40.5
	10.0	0.0500	2.03				
	10.0	0.1000	2.13	Acetate–Acetic Acid Buffers, Methanol-d			
	10.0	0.1500	2.42	$10^8[CH_3O^-]$, M			
p-Cl	8.0	0.0375	7.22	p-Cl	46.8	0.0300	1.95[b]
	8.0	0.0750	8.92		46.8	0.0750	3.25
	8.0	0.1125	10.26		46.8	0.1200	4.13
	7.0	0.0375	6.80		62.4	0.0750	4.99
	7.0	0.0750	8.49				
	7.0	0.1125	10.03				

[a] Ionic strength 0.1500 M (adjusted by addition of $LiClO_4$) in all runs. Standard deviations of rate constants are $\pm1.5\%$ (acetate buffers in CH_3OD), $\pm2.5\%$ (acetate buffers in CH_3OH), and $\pm5\%$ (phenoxide buffers in CH_3OH). [b] Rate constants are tabulated in min^{-1} for acetate buffers in CH_3OH and CH_3OD and in sec^{-1} for phenoxide buffers in CH_3OH.

Table II.[a] Catalytic Constants for Methanolysis of $XC_6H_4OSi(C_6H_5)_3$ in Methanol-h and Methanol-d at $27.4 \pm 0.1°$ ($\mu = 0.1500$ M)

X	Solvent	k_B, M^{-1} sec^{-1}			$10^5 k_0$,[b] sec^{-1}
		$CH_3CO_2^-$	$C_6H_5O^-$	CH_3O^-	
p-CH₃O	CH₃OH	2.62×10^{-5}	1.62	45.7	0.3
p-CH₃	CH₃OH	3.98×10^{-5}	1.15	50.0	0.2
H	CH₃OH	6.57×10^{-5}	3.61	94.0	-0.1
p-Cl	CH₃OH	71.3×10^{-5}	49.4	250	3.0
	CH₃OD	57.2×10^{-5}		185	
m-CF₃	CH₃OH	893×10^{-5}		3313	

[a] The catalyst constants are defined by eq 2. [b] These small terms presumably originate in experimental error, catalysis by trace impurities, or catalysis by solvent ("uncatalyzed" solvolysis).

observed in the organosilicon reaction are in complete consistency with the fact that small residual isotope effects are usually found after correction of "solvation rule" isotope effects for secondary contributions in aqueous solution.[3] These effects presumably arise from a combination of solvation-change isotope effects[5] and ones due to vibrational shifts on

formation of the strong hydrogen bonds of the catalytic site.[6]

Substituent Effects on Free Energy. The activation process under study here (eq 3) may be compared with the model process of eq 4 in order to assess the electronic conditions in the leaving group zone of the activated complex. The substituent effects on the free energy of activation ($\delta_x\Delta G^*$) and on the free energy of neutralization of the phenols[7] ($\delta_x\Delta G°$) would be expected to yield a relation (eq 5) the slope, m, of which should approximate the magnitude of q_2 (eq 3), the
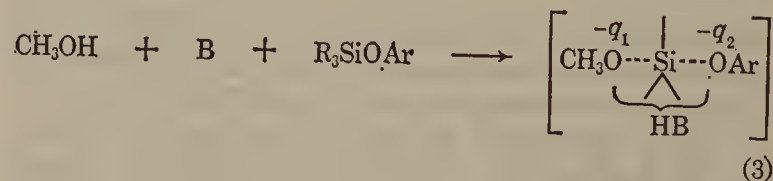
$$CH_3OH + B + R_3SiOAr \longrightarrow \left[CH_3O\cdots\underset{\underset{HB}{\wedge}}{\overset{-q_1}{Si}}\cdots OAr \right]^{-q_2}$$

(3)

$$B + HOAr \longrightarrow BH^+ + {}^-OAr$$ (4)

tronic conditions in the leaving group zone of the activated complex. The substituent effects on the free energy of activation ($\delta_x\Delta G^*$) and on the free energy of neutralization of the phenols[7] ($\delta_x\Delta G°$) would be expected to yield a relation (eq 5) the slope, m, of which should approximate the magnitude of q_2 (eq 3), the

$$\delta_x\Delta G^* = m\delta_x\Delta G°$$ (5)

charge on the activated complex leaving group.[8]

(5) C. G. Swain and R. F. W. Bader, *Tetrahedron*, 10, 182 (1960); C. G. Swain, R. F. W. Bader, and E. R. Thornton, *ibid.*, 10, 200 (1960); C. G. Swain and E. R. Thornton, *J. Am. Chem. Soc.*, 83, 3884, 3890 (1961).

(6) C. A. Bunton and V. J. Shiner, *ibid.*, 83, 42, 3207, 3214 (1961).
(7) These quantities were measured for methanol solution in this laboratory, using the spectrophotometric method given in the Experimental Section.
(8) J. E. Leffler and E. Grunwald, "Rates and Equilibria of Organic

It has been a frequent experience[9] that such simple interpretations of free energy correlation slopes (*e.g.*, the particularly straightforward interpretations of Brønsted parameters[3,8]) are difficult to reconcile with enthalpy–entropy data, when these are available. For example, the resonance and inductive effects usually attributed to remote substituents should both contribute to the observed enthalpies, whereas the actual situation in solution reactions is often that both enthalpies and entropies vary, sometimes in a complicated way.[10,11] Hepler's brilliant treatment[12] of phenol ionization resolves this difficulty for aqueous solution. He argues that (a) observed substituent effects on enthalpies are sums of internal energy contributions ($\delta\Delta H_{int}$, containing resonance and inductive effects) and of external contributions ($\delta\Delta H_{ext}$, chiefly due to solvation phenomena), as in eq 6; (b) no entropy changes are associated with $\delta\Delta H_{int}$, but[13] $\delta\Delta H_{ext} = 280\delta\Delta S_{ext}$ so that the free energy effect is given by eq 6b (since $\delta\Delta S_{ext} \approx \delta\Delta S$). The approximate equality of free

$$\delta\Delta H = \delta\Delta H_{int} + \delta\Delta H_{ext} \tag{6a}$$

$$\delta\Delta G = \delta\Delta H_{int} + (280 - T)\delta\Delta S \approx \delta\Delta H_{int} \tag{6b}$$

energy effects and internal effects arises at temperatures near 280°K and seems to underlie a great fraction of linear free energy relations in aqueous media.[14,15] In addition, it has been found possible to understand the substituent effect on the activation process for methoxide-catalyzed methanolysis of aryl methyl carbonates[16] and aryl acetates[17] by use of Hepler's ideas, with adoption of 320°K for the compensation temperature appropriate to solvation interaction in methanol. We therefore are reasonably confident of the interpretation of the present free energy data in internal energy terms.

Figure 1 shows a plot of $\delta_x\Delta G^*_B$ for methanolysis of aryloxytriphenylsilanes by three catalyzing bases, acetate ion, phenoxide ion, and methoxide ion, *vs.* $\delta_x\Delta G°$ for neutralization of phenols under the same conditions (data of Table III). The positive sign of *m* (eq 5) is expected (activated complex stabilization by
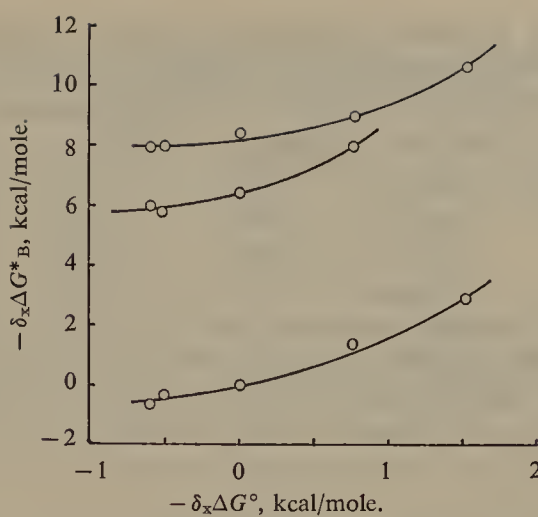
Figure 1. Substituent effect on the free energy of activation for methanolysis of aryloxytriphenylsilanes catalyzed by methoxide ion (top line), phenoxide ion (middle line), and acetate ion (bottom line) *vs.* substituent effect on the free energy of ionization of the corresponding arylol in methanol under the same conditions.

electron withdrawal), but the curvature is surprising.[18] Curvature of free energy relations for other reactions has been attributed to (a) a gross change in reaction mechanism with reactant structural variation,[19] (b) change in the rate-determining step of a multistep sequence as a function of reactant structure,[20] and (c) gradual variation in activated complex structure with reactant structure.[21] We shall consider these possibilities in turn.

Change in Mechanism. Two mechanisms are reasonably conceivable for this reaction:[1] a two-step, "Si-5" mechanism[22] (eq 7) and a concerted displacement process (eq 8). For the two-step mechanism, the k_1
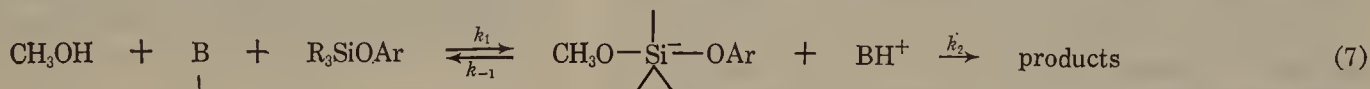
$$CH_3OH + B + R_3SiOAr \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} CH_3O{-}\overset{|}{\underset{\wedge}{Si}}{-}OAr + BH^+ \overset{k_2}{\longrightarrow} \text{products} \tag{7}$$

$$\overset{k_{ss}}{\longrightarrow} \left[\begin{matrix} CH_3 \\ O{\cdots}\overset{|}{\underset{\wedge}{Si}}{\cdots}O \\ BH \end{matrix}\right] \tag{8}$$

tion of the present free energy data in internal energy terms.

Figure 1 shows a plot of $\delta_x\Delta G^*_B$ for methanolysis of aryloxytriphenylsilanes by three catalyzing bases, acetate ion, phenoxide ion, and methoxide ion, *vs.* $\delta_x\Delta G°$ for neutralization of phenols under the same conditions (data of Table III). The positive sign of *m* (eq 5) is expected (activated complex stabilization by

step is probably[1] rate determining since ArO⁻ is a better leaving group[16] than CH_3O^-; more complex possibilities are discussed below. If the kinetics of a series of competing reactions are the same, the most general expression (eq 9) for the observed rate constant (k_o) is a sum of the rate constants, k_i, for the competing

$$k_o = \sum k_i \tag{9}$$

mechanisms. Converting to free energies and applying the substituent variation operator (δ_x), defining f_i (eq 12) as the fraction of the total reaction proceeding by

$$\Delta G^*_0 = -RT \ln \sum_i \exp(-\Delta G^*_i/RT) \tag{10}$$

Reactions," John Wiley and Sons, Inc., New York, N. Y., 1962, pp 156–161, and following. See also the discussion of the δ operator by these authors on p 26 of this book.

(9) *E.g.*, see P. G. Ashworth, "Catalysis and Inhibition of Chemical Reactions," Butterworth and Co. (Publishers) Ltd., London, 1963, Chapter I.

(10) Reference 8, Chapter 9.

(11) R. W. Taft, Jr., in "Steric Effects in Organic Chemistry," M. S. Newman, Ed., John Wiley and Sons, Inc., New York, N. Y., 1956.

(12) L. G. Hepler, *J. Am. Chem. Soc.*, **85**, 3089 (1963).

(13) The value of 280°K for the compensation temperature in water was taken from studies by R. F. Brown, *J. Org. Chem.*, **27**, 3015 (1962).

(14) E. M. Arnett and J. J. Burke, *J. Am. Chem. Soc.*, **88**, 4308 (1966).

(15) R. L. Schowen, *J. Pharm. Sci.*, in press.

(16) R. L. Schowen, C. G. Mitton, and J. Shapley, submitted for publication. See Abstracts of the 152nd National Meeting of the American Chemical Society, New York, N. Y., Sept 1966, Paper S139.

(17) C. G. Mitton and Michael Gresser, unpublished results.

(18) The curvature is well outside experimental error (see Table III). The same kind of curvature is also readily apparent on examination of the Hammett plots of E. Åkerman (*Acta Chem. Scand.*, **10**, 298 (1956); **11**, 373 (1957)) for the more complex reaction of basic aqueous ethanol with aryloxysilanes.

(19) Y. Okamoto and H. C. Brown, *J. Org. Chem.*, **22**, 485 (1957).

(20) W. P. Jencks, *Progr. Phys. Org. Chem.*, **2**, 63 (1964); J. F. Kirsch and W. P. Jencks, *J. Am. Chem. Soc.*, **86**, 833, 837 (1964).

(21) (a) C. G. Swain and W. P. Langsdorf, *ibid.*, **73**, 2813 (1951); (b) C. G. Swain and R. L. Schowen, *J. Org. Chem.*, **30**, 615 (1965).

(22) L. H. Sommer, "Stereochemistry, Mechanism and Silicon," McGraw-Hill Book Co., Inc., New York, 1965, p 131.

Table III.[a,b] Substituent Effects on Free Energies of Activation for Catalyzed Methanolysis of $XC_6H_4OSi(C_6H_5)_3(\delta_x\Delta G^*_B)$ and on Dissociation of XC_6H_4OH in Methanol $(\delta_x\Delta G°)$

X	$\delta_x\Delta G^*_{CH_3CO_2}-$	$\delta_x\Delta G^*_{C_6H_5O}-$	$\delta_x\Delta G^*_{CH_3O}-$	$\delta_x\Delta G°$
p-CH_3O	+0.54	−6.01	−7.98	0.60
p-CH_3	+0.29	−5.80	−8.05	0.51
H	0.0	−6.47	−8.43	0.0
p-Cl	−1.40	−8.04	−9.00	−0.77
m-CF_3	−2.90		−10.52	−1.52

[a] Rate data are for $27.4 \pm 0.1°$, equilibrium data for $25.0 \pm 0.1°$. All numbers are in kcal/mole; errors are about ± 0.03 kcal/mole. [b] Rate data are relative to $\Delta G^*_{CH_3CO_2}-$, $C_6H_5OSi(C_6H_5)_3$; equilibrium data are relative to $\Delta G°$, C_6H_5OH.

$$\delta_x\Delta G^*_0 = \sum_i \delta_x\Delta G^*_i \exp(-\Delta G^*_i/RT)/$$

$$\sum_i \exp(\Delta G^*_i/RT) \quad (11)$$

$$f_i \equiv \exp(-\Delta G^*_i/RT)/\sum_i \exp(-\Delta G^*_i/RT) \quad (12)$$

$$\delta_x\Delta G_0 = \sum_i f_i\delta_x\Delta G_i \quad (13)$$

$$\delta_x\Delta G^*_i = m_i\delta_x\Delta G° \quad (14)$$

$$\delta_x\Delta G^*_0 = \left(\sum_i f_im_i\right)\delta_x\Delta G° = m_0\delta_x\Delta G° \quad (15)$$

the ith mechanism, and assuming a rate–equilibrium correlation (eq 5) for each mechanism (eq 14), we obtain finally eq 15. This shows the observed correlation slope to be an average of the slopes appropriate to the contributing mechanisms, each weighted by the fraction of the reaction proceeding by the corresponding mechanism. Of course, the f_i should also change with reactant structure (as measured by $\delta_x\Delta G°$; notice that $-\delta\Delta G°$ and $-\delta_x\Delta G^*_B$ are plotted in Figure 1) and this function is obtained by application of δ_x to eq 12 and introduction of eq 14 to the result, yielding eq 16. Thus, the more positive m_i, the smaller its contribution

$$\delta_x f_i = \frac{f_i}{RT}\{m_0 - m_i\}\delta_x\Delta G_0 \quad (16)$$

to m_0 will become as $\delta_x\Delta G°$ increases. In the present case, m_{ss} (for the single-step mechanism) should be larger than m_{ts} (two-step mechanism) because the Si–O bond is breaking (and negative charge is thus appearing in the leaving-group oxygen) in the single-step mechanism, whereas this bond is not breaking in the (rate-determining) activated complex, for the addition step, in the two-step reaction. Therefore at large $\delta_x\Delta G°$ (poor leaving groups), $m_0 \approx m_{ts}$, while at small $\delta_x\Delta G°$ (good leaving groups), $m_0 \approx m_{ss}$. Thus as $\delta_x\Delta G°$ increases, m_0 should go from large values (m_{ss}) to small values (m_{ts}), as is observed.

The observed substituent effects are compatible with a change in mechanism from a single-step displacement (eq 8) with good leaving groups to a two-step displacement (eq 7) with poor leaving groups.

Change in the Rate-Determining Step. Let us now consider the possibility that the curvature in Figure 1 arises from a change in the rate-determining step of a two-step sequence (eq 7). This seems initially unlikely since *any* ArO⁻ would be expected to exceed CH₃O⁻ in leaving-group tendency, at least on polar grounds,[16] and thus the k_1 step of eq 7 would effectively determine the rate if $k_2 > k_{-1}$. However, the hypothetical "Si-5"

intermediate may constitute a species of considerable steric compression[22] and the (probably) greater bulk of the ArO⁻ groups might compete with the polar effect.[23] This hypothesis must therefore be discussed.

Application of the steady-state method[24] to eq 7 yields eq 17 for the observed rate constant. Proceeding

$$k_0 = \frac{k_1k_2}{k_{-1} + k_2}$$

$$k_0^{-1} = k_1^{-1} + \left(\frac{k_1}{k_{-1}}k_2\right)^{-1} \quad (17)$$

as in the last section, we obtain eq 18, where f_2 and f_{-1}, defined by eq 19, are respectively the fractions

$$\delta_x\Delta G^*_0 = f_2\delta_x\Delta G^*_1 + f_{-1}\delta_x\Delta G^*_2 \quad (18)$$

$$f_2 = \exp(\Delta G^*_1/RT)/[\exp(\Delta G^*_1/RT) + \exp(\Delta G^*_2/RT)] \quad (19a)$$

$$f_{-1} = \exp(\Delta G^*_2/RT)/[\exp(\Delta G^*_1/RT) + \exp(\Delta G^*_2/RT)] \quad (19b)$$

$$f_2 + f_{-1} = 1 \quad (19c)$$

of the "Si-5" intermediate which proceed on to products and return to reactants; here ΔG^*_1 is the free energy of activation for conversion of reactants into the first ("addition") activated complex and ΔG^*_2 that for conversion of *reactants* into the second ("elimination") activated complex. Equation 18 shows the observed substituent effect to be an average of effects for formation of the two activated complexes, each weighted by the fraction of intermediate which decomposes by the *other* route. Again, assuming each of the composite processes to show a rate–equilibrium correlation, and introducing eq 19c, we have eq 20 (where m_i corresponds to ΔG^*_i).

$$\delta_x\Delta G^*_0 = (m_2 + f_2[m_1 - m_2])\delta_x\Delta G° = m_0\delta_x\Delta G° \quad (20)$$

On chemical grounds we argue that both m_1 and m_2 will be positive (since both activated complexes are electron rich relative to reactants) and that $m_2 > m_1$ since the Si–O bond is breaking in the m_2 process. Thus, from eq 20, the slope observed should be positive but should decrease as f_2 becomes larger. In the same way as above, eq 21 is found for the effect of structure on

$$\delta_x f_2 = \left[\frac{f_2(1 - f_2)}{RT}(m_1 - m_2)\right]\delta_x\Delta G° \quad (21)$$

f_2. As $\delta_x\Delta G°$ increases (poorer leaving group), f_2 decreases; thus m_0 should increase as $\delta_x\Delta G°$ becomes larger. This is contrary to the observations of Figure 1 and this hypothesis is therefore incompatible with the data.

Changes in Activated Complex Structure. Considerable evidence[25] indicates that activated complexes are more sensitive in their gross structural parameters and electron distributions than are stable molecules. Thus, although remote groups rarely exert large effects on bond lengths, angles, etc., in reactant molecules, these influences may appear in activated complexes. It

(23) Larger groups appear to be expelled with less facility than smaller groups from the tetrahedral intermediates of ester solvolysis: S. C. Hoops, Ph.D. Thesis, University of Kansas, 1967.

(24) A. A. Frost and R. G. Pearson, "Kinetics and Mechanism," 2nd ed, John Wiley and Sons, Inc., New York, N. Y., 1962.

(25) See discussions in ref 3, 21, and 26–28.

should be possible to predict the direction of such effects by using (a) the extended Hammond postulate[26] (EHP), (b) the Swain–Thornton reacting bond rule[27] (STR), and (c) the Thornton perturbation method[28] (TPM).

On the concerted-reaction model (eq 8), all approaches (EHP, STR, and TPM) predict that increasing electron donation (larger $\delta_x\Delta G°$) will lengthen the activated complex Si$\cdots$OAr bond, increasing the degree of negative charge in the leaving group zone (q_2, eq 3). If m is a measure of q_2 it would be increased, leading to a concave-downward curvature, as opposed to the concave-upward curvature observed in Figure 1. On the two-step model (eq 8), the first step should be rate determining (as explained above) and little change in m with leaving group structure is expected. Nevertheless, some change could result from variations in the position of the center of negative charge density or from differences in release of electron density onto the leaving group from oxygen dπ–pπ conjugation[29] with Si. Both the EHP and TPM predict that CH$_3$O-$\cdots$Si will be shorter with poorer leaving groups (electron donation, larger $\delta_x\Delta G°$), which should lead to a center of negative charge closer to the substituents and greater release of electron density from the Si 3d orbitals and thus a larger m at larger $\delta_x\Delta G°$, again contrary to the observations.

The STR predicts, on the other hand, that electron donation will lengthen the CH$_3$O$\cdots$Si bond. This prediction is disturbing since it contains an internal contradiction for the general case of attack of various nucleophiles N on a substituted organosilicon species, RSiR$'_3$. If the Swain–Scott equation[30] (eq 22) describes the dependence of the rate on the nucleophilicity of N and the Hammett equation (eq 23) the influence

$$\log k_{RN} = S_R n_N + \log k_{RN_0} \qquad (22)$$

$$\log k_{RN} = \rho_N \sigma_R + \log k_{R_0N} \qquad (23)$$

of R then, as Miller[31] has shown, a relation exists between the parameters (eq 24). The values of S_R for various substrates must be linear in σ_R and the ρ_N for various nucleophiles must be linear in n_N *with the*

$$(S_R - S_{R_0})/\sigma_R = (\rho_N - \rho_{N_0})/n_N = C \qquad (24)$$

same slope, C. The sign of this slope is predictable from the EHP, the STR, or the TPM; the arguments have been developed for carbonyl addition reactions by Jencks and Cordes[32] and the relations experimentally confirmed by do Amaral, Sandstrom, and Cordes.[33] According to the EHP or the TPM, electron withdrawal in R (larger σ_R) should lengthen N$\cdots$Si, leading to smaller S_R. An increase in n_N should also lengthen

N$\cdots$Si, giving a more negative ρ_N. Thus C should be negative by both arguments. The STR predicts that electron withdrawal in R will *shorten* N$\cdots$Si, increasing S_R (positive C), but also predicts that an increase in n_N will lengthen N$\cdots$Si, giving a more negative ρ_N (negative C). We therefore defer to the predictions of the EHP and the TPM in this case.[34]

Role of dπ–pπ Bonding and Its Implications. A plot of Jaffé's values[35] for the (3d,2p)-π overlap integral as a function of internuclear distance reveals a sharp falloff beyond the reactant Si–O distance[36] of 1.63 A. It may well be, therefore, that if substitution in the aryl group induces changes in the activated complex Si–O distance, concomitant variations in dπ–pπ bonding may occur. Such a model can, in fact, account for the shape of the free energy curve of Figure 1.

Assume that the free-energy curve excluding π-bonding effects has the linear form of the dashed line in Figure 2. This is reasonable since the slope is intermediate between the extremes of $m \sim 0$ and $m \sim 1.2$ for the curves of Figure 1, as would be expected for an activated complex with a partially broken Si–OAr bond. Further assume that, with good leaving groups, the activated complex Si–OAr bond is sufficiently short that π bonding is still important, but that as the leaving group becomes worse and the bond lengthens, this bonding is lost. This would produce the deviation shown by the solid line on the right side of Figure 2, with good leaving groups being unusually good but with the π-bonding effect being gradually lost until the two curves finally intersect at the point where π bonding is unimportant in the activated complex. As the Si–OAr bond is lengthened, however, the CH$_3$O–Si bond is simultaneously shortened. At some point, it should become short enough that π bonding enters the picture for this bond and the deviation shown at the left of Figure 2 will now result. Thus variations in dπ–pπ bonding in the activated complex can account for the observed curvature in the free energy relations.

If this postulate is reasonable, similar observations should be made in other, related systems. Actually, the data of Åkerman[18] for aryloxysilane solvolysis in aqueous ethanol show an exactly comparable curvature. So do the data of Eaborn and Walton[37] for cleavage of (C$_2$H$_5$)$_3$SiC≡CAr in methanol–water. On the other hand, no curvature appears in Hammett plots for cleavage of substituted benzyl groups from silicon,[38] a happy result since no π interactions are expected in this case of a saturated-carbon leaving group.

Furthermore, the phenomenon should also appear in leaving group reactivities from other second-row centers such as phosphorus. The results are: (a) for ROPO$_3^{2-}$, the free energies of activation are a good linear function[39] of leaving group pK_a; (b) for ROPO$_3$H$^-$, there is concave-downward curvature[39] so that good leaving groups are *less* reactive than pre-

(26) (a) G. S. Hammond, *J. Am. Chem. Soc.*, 77, 334 (1955); (b) K. B. Wiberg, *Chem. Rev.*, 55, 733, 737 (1955); (c) A. Streitwieser, Jr., *ibid.*, 56, 571 (1956).

(27) C. G. Swain and E. R. Thornton, *J. Am. Chem. Soc.*, 84, 817 (1962).

(28) (a) E. R. Thornton, *ibid.*, 89, 2915 (1967).

(29) Good evidence for such conjugation exists: (a) C. Eaborn, "Organosilicon Compounds," Butterworth & Co. (Publishers) Ltd., London, 1960, p 94 ff; (b) R. West, L. S. Watley, and K. J. Lake, *J. Am. Chem. Soc.*, 83, 761 (1961).

(30) C. G. Swain and C. B. Scott, *ibid.*, 75, 141 (1953).

(31) S. I. Miller, *ibid.*, 81, 101 (1959).

(32) Reviewed by W. P. Jencks, *Progr. Phys. Org. Chem.*, 2, 63 (1964).

(33) L. do Amaral, W. A. Sandstrom, and E. H. Cordes, *J. Am. Chem. Soc.*, 88, 2225 (1966).

(34) The apparent experimental support for the STR prediction for carbonyl addition (L. B. Jones and T. M. Sloane, *Tetrahedron Letters*, 831 (1966)) can be understood if the entropy of the activated complex does not decrease monotonically with a decrease in the nucleophile–carbonyl distance. This now seems probable.[23]

(35) H. H. Jaffé, *J. Chem. Phys.*, 21, 259 (1953).

(36) Reference 29a, p 492.

(37) C. Eaborn and D. M. R. Walton, *J. Organometal. Chem.* (Amsterdam), 4, 217 (1965).

(38) C. Eaborn and S. H. Parker, *J. Chem. Soc.*, 126 (1955).

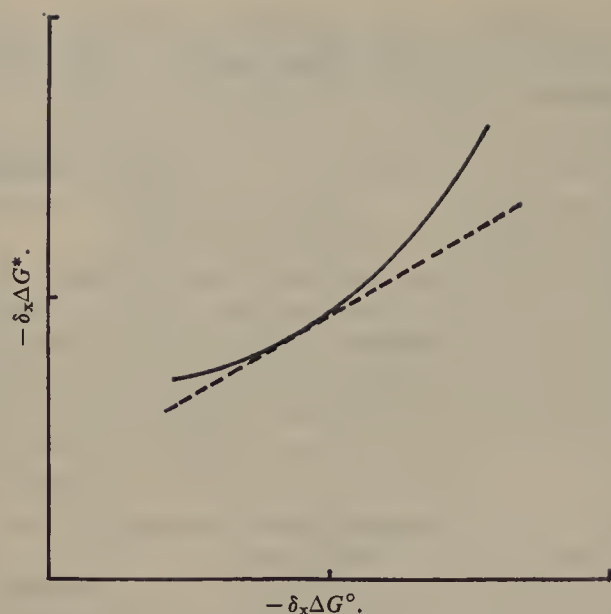(39) A. J. Kirby and A. G. Varvoglis, *J. Am. Chem. Soc.*, 89, 415 (1967), and other papers cited there.

Figure 2. Hypothetical linear free energy relation for aryloxy-silane methanolysis (dashed line) modified by changes in π bonding of Si to leaving group (deviation on right-hand side) and entering group (deviation on left-hand side). Compare the solid line with Figure 1.

dicted; (c) for $CH_3PO(OC(CH_3)_2H)OAr$, the reactivities for various Ar are given[40] as $p\text{-}NO_2C_6H_4 > p\text{-}ClC_6H_4 > C_6H_5 \simeq CH_3OC_6H_4$. Result c for the phosphonate diester is in good accord with our hypothesis. Result a can be rationalized by assuming the phosphorus 3d orbitals to be saturated by the three O^- substituents so that π bonding to RO is not important. Result b is explained by Kirby and Varvoglis as being due to a change in mechanism with leaving group from rate-determining decomposition of $^-O_3P^+(OHR)$ to its rate-determining formation. This may well mask the π-bonding effect. We conclude that the data for phosphorus compounds are not in disagreement with the π-bonding hypothesis.

Conclusion

The isotope effect and substituent effect data for methanolysis of aryloxysilanes are in accord with a general base catalyzed process of the "solvation rule" class in which the leaving group substituent effect varies with leaving group from practically nil ($m \sim 0$) to very large values ($m \sim 1.2$). The latter phenomenon may result from either (i) a change in mechanism from an "Si-5" process[41] to an S_N2 process or (ii) variations in Si–O $d\pi$–$p\pi$ bonding in the activated complex.

Although the data do not decide conclusively between these possibilities, we favor ii as more consistent with the limiting values of m found from Figure 1. If i were correct, we would expect a larger effect than $m \sim 0$ for formation of the Si-5 species, by analogy with carbonyl addition[16,17] where the corresponding slope is 0.6. We would also expect a smaller value than 1.2 for the S_N2 mechanism, since the ArO bond should not be very completely broken, as argued above.[42]

(40) Data of J. Epstein, cited by J. O. Edwards, "Inorganic Reaction Mechanisms," W. A. Benjamin, Inc., New York, N. Y., 1964, p 63.
(41) Or an "S_N2^*–Si-5" process: see ref 22 and also L. H. Sommer, G. A. Parker, N. C. Lloyd, C. L. Frye, and K. W. Michael, *J. Am. Chem. Soc.*, 89, 857 (1967).
(42) A value larger than unity is conceivable, however, because of contribution of structures such as i to the reactant hybrid.

$$>Si^-\!\!=\!\!O^+\!\!-\!\!Ar$$
$$i$$
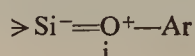
On the other hand, practically any limiting slopes could result from ii, including an inversion to a negative slope with sufficiently electron-donating substituents.

Experimental Section

Materials. Anhydrous sodium acetate (Fisher Certified), lithium perchlorate (G. Frederick Smith), and lithium chloride (Fisher Certified) were dried at 105° for 48 hr and stored over silica gel. Sodium methoxide solutions were prepared by dissolving freshly cut sodium in methanol and were standardized against potassium acid phthalate (Baker and Adamson Primary Standard).

Phenoxytriphenylsilane, p-chlorophenoxytriphenylsilane, p-methoxyphenoxytriphenylsilane, and (p-methylphenoxy)triphenylsilane were synthesized using the method described by Larsson[43] in which ethanol is distilled from a refluxing mixture of ethoxytriphenylsilane, the appropriate phenol, and a small piece of sodium. Fractional vacuum distillation of the resulting dark brown solid, followed by recrystallization from petroleum ether (bp 30–70°), gave the desired silane.

(m-Trifluoromethylphenoxy)triphenylsilane was prepared from chlorotriphenylsilane and the appropriate phenol with pyridine acting as a hydrogen chloride acceptor, following a procedure similar to that of Gerrard and Kilburn.[44] To obtain the m-trifluoromethylsilane, 0.1 mole of chlorotriphenylsilane (Peninsular Chemical Co.) dissolved in petroleum ether (bp 60–110°) was added dropwise to a solution of 0.1 mole of m-trifluoromethylphenol (Pierce Chemical Co.) and 0.1 mole of pyridine (Fisher reagent grade) in petroleum ether (bp 60–110°). After refluxing the solution for 2 hr, the pyridine hydrochloride was filtered off and the solvent removed. Fractional vacuum distillation followed by recrystallization from petroleum ether (bp 30–60°) gave the silane in 86% yield, mp 60.5–61.0°.

Methanol-d. CH_3OD was synthesized from dimethyl carbonate (Eastman White Label), deuterium oxide (Bio-Rad), and dimethyl sulfate catalyst (Mallinckrodt OR), following the procedure described by Streitwieser, Verbit, and Stang.[45] The final distillation from sodium was performed as the methanol-d was needed. Vapor phase chromatography using a Carbowax 20M column indicated no impurities in the final product.

Kinetic Measurements and Data Treatment. Absorption measurements were made on either a Cary Model 14 spectrophotometer or a Beckman DB spectrophotometer with attached log potentiometric recorder. The latter instrument was also equipped with a constant-temperature cell block which was used when samples had to be left in the instrument for a sustained length of time. A matched set of four glass-stoppered Pyrocell silica cells were used in obtaining the absorption readings. Constant temperature was maintained by use of a thermostatically controlled water bath in which flasks could be immersed. A recirculating pump was used to maintain a flow of water through the spectrophotometer constant-temperature block. Temperatures were maintained within 0.1° of the stated value.

Observed first-order rate constants were calculated by means of the integrated form of the first-order kinetic rate law, using a least-squares method and the IBM 7040 computer.

Kinetic Procedures. Wavelengths (mμ) used for following the kinetic progress of each reaction were (substrate, method A, method B): $p\text{-}CH_3OC_6H_4OSi(C_6H_5)_3$, 390, 286.5; $p\text{-}CH_3C_6H_4OSi(C_6H_5)_3$, 280, 283.0; $C_6H_5OSi(C_6H_5)_3$, 271.8, 266.0; $p\text{-}ClC_6H_4OSi(C_6H_5)_3$, 284.0, 277.0; $m\text{-}CF_3C_6H_4OSi(C_6H_5)_3$, 285.0, —.

A. Acetate Buffers. Methanolysis reaction rates were determined by spectrophotometrically following the increase in ultraviolet absorption due to formation of the phenol product. The aryloxysilane reactant was dissolved in the acetate buffer of desired strength, using a glass-stoppered volumetric flask; this flask was thermostated at 27.4° and samples were withdrawn periodically for ultraviolet absorption analysis. In the cases of the m-trifluoromethyl reactant and of solvolysis in CH_3OD, this procedure was modified by transferring a sample of the reaction solution to the stoppered ultraviolet cell, which was inserted into the constant-temperature block of the Beckman spectrophotometer; absorption readings were then made on a continuous basis.

B. Phenoxide Buffers. Determination of the methanolysis reaction rates was made by spectrophotometrically measuring the
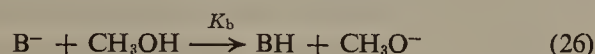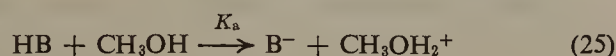
(43) E. Larsson, *Chem. Ber.*, 86, 1382 (1953).
(44) W. Gerrard and K. D. Kilburn, *J. Chem. Soc.*, 1536 (1956).
(45) A. Streitwieser, Jr., L. Verbit, and P. Stang, *J. Org. Chem.*, 29, 3706 (1964).

decrease in aryloxysilane concentration after simultaneously quenching the reaction and removing the phenoxide buffer by means of an extraction technique.

Stock solutions of reactant silane dissolved in 0.1500 M LiClO$_4$ in methanol solution and of phenoxide buffer were thermostated at 27.4°; both of these solutions were double the concentration desired in the reaction solution. Five milliliters of each solution was rapidly mixed in a 50-ml flask, and after the desired interval of time the reaction was quenched in an extraction solution of 10 ml of cyclohexane (practical grade) and 10 ml of aqueous sodium hydroxide, sufficiently basic to neutralize all the phenol present. After separation of the two phases, the cyclohexane solution was further extracted with 10 ml of dilute aqueous HCl and with 5 ml of distilled water, dried with anhydrous sodium sulfate, and subjected to the absorbance analysis. Control experiments showed the silane–phenol buffer separation to be quantitative; rate constants using this procedure were obtained for the p-chlorosilane reactant in acetate buffer and were identical with those obtained using method A.

Acid–Base Equilibria in Methanol. The dissociation constants K_a and K_b as defined by eq 25 and 26 were derived for acetic acid,

$$\text{HB} + \text{CH}_3\text{OH} \xrightarrow{K_a} \text{B}^- + \text{CH}_3\text{OH}_2^+ \qquad (25)$$

$$\text{B}^- + \text{CH}_3\text{OH} \xrightarrow{K_b} \text{BH} + \text{CH}_3\text{O}^- \qquad (26)$$

phenol, and m-trifluoromethylphenol in methanol solvent. These measurements were carried out at 27.4° and an ionic strength of 0.1500 M so as to duplicate the environment in which the methanolysis reactions were conducted. The results obtained using the methods described below are tabulated in Table IV.

Table IV.[a] Equilibrium Constants in Methanol at $27.4 \pm 0.1°$ ($\mu = 0.1500$ M)[b]

HA	pK_b	pK_a
CH$_3$CO$_2$H	7.48	9.44
C$_6$H$_5$OH	2.66	14.26
m-CF$_3$C$_6$H$_4$OH	3.76	13.16

[a] pK_b determined experimentally; pK_a calculated from $pK_{\text{auto}}(\text{CH}_3\text{OH}) = 16.92$ (E. Grunwald and E. Price, *J. Am. Chem. Soc.*, **86**, 4517 (1964)). [b] Maintained by added LiClO$_4$.

K_b of Phenol. A series of phenol–phenoxide buffers was prepared from phenol and sodium methoxide solution with [added phenol] $\simeq 4 \times 10^{-4}$ M and [added methoxide] varying between 0.01 and 0.04 M. The absorbance A of each buffer was measured at 288 mμ, a wavelength at which phenoxide ion is the only absorbing species. These data were fitted to eq 27, derived by Stearns

$$\frac{[\text{added phenol}]}{A} = \frac{1}{k''} + \frac{K_b}{k''} \frac{1}{[\text{MeO}^-]} \qquad (27)$$

and Wheland,[46] using a least-squares plot of 1/[MeO$^-$] *vs.* [added phenol]/A; from the slope K_b/k'' and intercept $1/k''$, K_b can be determined. [MeO$^-$], however, is not accurately known because of phenoxide solvolysis, so [MeO$^-$] was redetermined using the calculated K_b value and a new plot was made. This iteration procedure was continued, using an IBM 7040 computer, until K_b remained constant on successive calculations $(([K_2 - K_1]/K_2) < 0.0001)$.

K_b of m-Trifluoromethylphenol. The same mathematical procedure described above was used for this determination. The buffer solution had [added m-trifluoromethylphenol] $= 2.37 \times 10^{-4}$ M and [added methoxide] $= (2–8) \times 10^{-4}$ M; the wavelength used was 300 mμ. Before preparing the buffer solutions, the m-trifluoromethylphenol (Pierce Chemical Co.) was purified by vacuum distillation since the reagent grade chemical was unavailable.

K_b of Acetic Acid. The method used in this determination was calculation of K_b for an indicator, in this case bromocresol green (BCG), and utilization of this value in conjunction with acetate buffers containing BCG indicator. K_b of acetic acid was derived by use of eq 28 and 29.

$$\text{HInd} + \text{OAc}^- \underset{}{\overset{K'}{\rightleftharpoons}} \text{Ind}^- + \text{HOAc}$$

$$\frac{[\text{Ind}^-][\text{HOAc}]}{[\text{HInd}][\text{OAc}^-]} = K' \qquad (28)$$
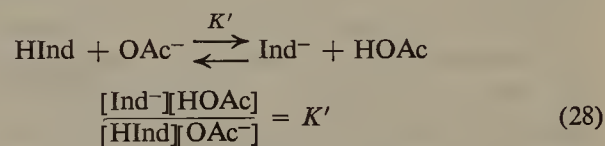
$$pK_b(\text{HOAc}) = pK_b(\text{HInd}) + pK' \qquad (29)$$

A stock indicator solution was prepared by dissolving in methanol a weighed sample of the disodium salt of BCG (Matheson Coleman and Bell), previously dried at 105°; using added sodium methoxide to ensure complete conversion to the basic form (Ind$^-$), a molar extinction coefficient ϵ of 3.81×10^4 was determined at 617 mμ, a wavelength at which the acidic form (HInd) does not absorb. K_b for BCG was calculated using the observed absorbance A at 617 mμ assuming that [HInd] = [MeO$^-$]. A value of $K_b(\text{BCG}) = 1.70 \times 10^{-8}$ ($pK_b = 7.770$) was obtained.

Three acetic acid–acetate buffers containing known [added BCG] were prepared and their absorbance was measured at 617 mμ. An average K' value of 1.932 ± 0.015 ($pK' = -0.286 \pm 0.003$) was derived, leading to a pK_b value of 7.484 for acetic acid.

K_b of Acetic Acid in Methanol-d_1. The procedure described in the preceding section was repeated using methanol-d_1 as the solvent. The various calculated constants in the medium are: $\epsilon = 3.911 \times 10^4$; $K' = 1.856$; $pK' = -0.269$; $K_b(\text{BCG}) = 2937 \times 10^{-8}$; $pK_b(\text{BCG}) = 7.532$; $pK_b(\text{HOAc}) = 7.263$.

(46) R. S. Stearns and G. W. Wheland, *J. Am. Chem. Soc.*, **69**, 2025 (1947).

2-Oxo-1,3-alkadiyl Diradicals. Dehalogenation of α,α'-Dihalo Ketones with Potassium Vapor[1,2]

Robert G. Doerr and Philip S. Skell

Contribution from the Department of Chemistry, The Pennsylvania State University, University Park, Pennsylvania 16802. Received April 7, 1967

Abstract: 2-Oxo-1,3-alkadiyl diradicals were prepared by the gas-phase reaction of α,α'-dihalo ketones with potassium vapor. The diradicals cyclize to cyclopropanones, which decarbonylate under the reaction conditions to give the olefin residue. The preparation of 2,2-dimethoxy-1,3-propadiyl diradical by the reaction of the corresponding dichloride and potassium vapor results in the isolation of dimethyl ketal of cyclopropanone.

The 2-oxo-1,3-alkadiyl diradicals (or the corresponding zwitterions) have been proposed as intermediates in the Favorsky rearrangement[3] and in the photolysis of 1,3-cyclobutanediones.[4] The products obtained from the photolysis of tetrasubstituted 1,3-cyclobutanediones consist of the tetrasubstituted olefin and carbon monoxide, suggesting that the initial diradical cyclizes to the cyclopropanone, and the latter decarbonylates.[4a,b] Photolysis of tetramethyl-1,3-cyclobutanedione in furan resulted in the trapping of the cyclopropanone or the 2-oxo-1,3-diradical as a furan adduct,[4c,d] and photolysis in the presence of oxygen indicates that the intermediate of this reaction acts as a biradical toward oxygen.[4b,e] Tetramethylcyclopropanone in a pentane solution reacts with furan or oxygen, but is stable in the absence of these reactants.[4f]

The reactions of 1,3-dihaloalkanes with alkali metal vapor lead to 1,3-alkadiyl diradicals which cyclize to cyclopropanes in over-all yields up to 85%.[5] We report here the reaction of α,α'-dihalo ketones with alkali metal vapor under similar conditions as a method of investigating the intermediate 2-oxo-1,3-alkadiyl diradicals. The reaction of 1,3-dichloropropanone with sodium vapor was studied in the past, but the only information obtained was that the reaction occurs with a weak luminescence.[6] However, relevant information was derived from the reaction of chloroacetone with sodium vapor. The collision yield is 0.1–0.2, indicating that less than ten collisions are necessary per reaction event.[7] The isolation of biacetonyl as a product of the reaction proved the intermediacy of acetonyl radicals.[8]

2-Oxo-1,3-propadiyl and 2,2-Dimethoxy-1,3-propadiyl

2-Oxo-1,3-propadiyl diradical (3) was generated by the reaction of potassium vapor[9] with 1,3-dichloropropanone (1). The results of this reaction are presented in Table I. The mole ratios of the components are

Table I. Major Products Obtained from the Reaction of 1,3-Dichloropropanone with K

Products	Reaction 1[a]	Reaction 2	Reaction 3
	Temp, °C 295–303	272–281	257–265
	Mole ratios		
Carbon monoxide		12.4	10.8
Methane		19.1	35.2
Ethane	3.3	15.2	6.6
Ethene	88.1	50.4	44.0
Propene	1.2	1.3	1.9
	92.6	98.4	98.5
Yield of ethene, %	33.3	16.2	11.9

[a] Methane and carbon monoxide were not collected.

also equal to the mole per cent of the total product. The amount of carbon monoxide recovered from the reaction would be decreased by the secondary reaction of carbon monoxide with potassium.[10]
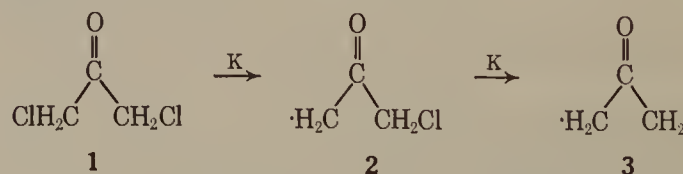
The high yield of ethene and the presence of carbon monoxide can be explained by the cyclization of the 1,3-diradical 3 to cyclopropanone (4), followed by a thermal decarbonylation of cyclopropanone to ethene (*vide infra* for a discussion of the energetics).

(1) From the Ph.D. Thesis of R. Doerr.
(2) This work was supported by the National Science Foundation.
(3) (a) A. S. Kende, *Org. Reactions*, **11**, 261 (1960); (b) J. G. Aston and J. D. Newkirk, *J. Am. Chem. Soc.*, **73**, 3900 (1951); (c) J. G. Burr and M. J. S. Dewar, *J. Chem. Soc.*, 1201 (1954); (d) H. O. House and W. F. Gilmore, *J. Am. Chem. Soc.*, **83**, 3980 (1961); (e) H. O. House and W. F. Gilmore, *ibid.*, **83**, 3972 (1961); (f) A. W. Fort, *ibid.*, **84**, 2620 (1962); (g) *ibid.*, **84**, 4979 (1962); (h) *ibid.*, **84**, 2625 (1962); (i) R. C. Cookson and M. J. Nye, *J. Chem. Soc.*, 2009 (1965); (j) R. C. Cookson and M. J. Nye, *Proc. Chem. Soc.*, 129 (1963); (k) W. B. Hammond and N. J. Turro, *J. Am. Chem. Soc.*, **88**, 2880 (1966).
(4) (a) N. J. Turro, G. W. Byers, and P. A. Leermakers, *ibid.*, **86**, 955 (1964); (b) N. J. Turro, P. A. Leermakers, H. R. Wilson, D. C. Neckers, G. W. Byers, and G. F. Vesley, *ibid.*, **87**, 2613 (1965); (c) H. G. Richey, J. M. Richey, and D. C. Clagett, *ibid.*, **86**, 3906 (1964); (d) R. C. Cookson, M. J. Nye, and G. Subrahmanyam, *Proc. Chem. Soc.*, 144 (1964); (e) P. A. Leermakers, G. F. Vesley, and N. J. Turro, *J. Am. Chem. Soc.*, **86**, 4213 (1964); (f) N. J. Turro, W. B. Hammond, and P. A. Leermakers, *ibid.*, **87**, 2775 (1965).
(5) P. S. Skell and E. J. Goldstein, unpublished work; E. J. Goldstein, Ph.D. Thesis, The Pennsylvania State University, 1964.
(6) C. E. H. Bawn and W. J. Dunning, *Trans. Faraday Soc.*, **35**, 185 (1939).
(7) E. Warhurst, *Quart. Rev.* (London), **5**, 44 (1951).
(8) J. N. Haresnape, Thesis, University of Manchester, quoted by C. E. H. Bawn, *Ann. Rept. Progr. Chem.* (Chem. Soc. London), **39**, 36 (1942).
(9) The predominant reacting species in the previously described sodium–potassium alloy spray apparatus would be monatomic potassium: P. S. Skell, E. J. Goldstein, R. J. Petersen, and G. L. Tingey, *Ber.*, **100**, 1442 (1967).
(10) F. Ephraim, "Inorganic Chemistry," 6th ed, Oliver & Boyd, Ltd., London, 1954, p 827.

Employing the same reaction conditions, the dimethyl ketal of 1,3-dichloropropanone (6) is converted in 11% yield to 1,1-dimethoxycyclopropane (8), a ketal of cyclopropanone. The products (and their mole ratio) obtained from the reaction of 1,3-dichloro-2,2-di-

methoxypropane with potassium vapor at 246–262° are: 1,1-dimethoxycyclopropane (24.7), 2-methoxypropene (11.9), allene (3.3), propene (34.1), propane (1.4), ethene (0.5), ethane (0.7), and methane (16.6). Under the reaction conditions allene is converted primarily to nonvolatile material, and, in low yields, to propene and propane. Thus, allene formation is a substantial reaction. Stoichiometrically the formation of allene involves the elimination of two methoxy radicals from the 1,3-diradical 7. The decomposition of 7 to the methoxy radicals and allene is unlikely. The first methoxy elimination would lead to 9 in an approximately thermoneutral step (~ -60 kcal for double bond formation, ~ -20 kcal for allylic stabilization, and $\sim +80$ kcal for carbon–oxygen bond cleavage). With these same values the second step is 40 kcal endothermic. It is more probable that the formation of allene is due to reaction of the 1,3-diradical 7 with potassium atoms resulting in the elimination of potassium methoxide from the reaction complex.[11] Acquisition of a hydrogen atom by the monoradical 9 would give 2-methoxypropene.

1,1-Dimethoxycyclopropane was identified on the basis of the following evidence: the infrared spectrum resembled closely that of the corresponding diethoxy compound;[12] the mass spectrum had a parent peak at m/e 102; the nmr spectrum consisted of two singlets at 0.76 and 3.29 ppm (δ scale) in a respective ratio of 2:3. 2-Methoxypropene was identified by comparison of its infrared spectrum and its vpc retention time with that of an authentic sample.

2-Oxo-3-methyl-1,3-butadiyl

The major products from the reaction of 1,3-dibromo-3-methyl-2-butanone (11) with potassium vapor at 217–232° are (mole ratios): carbon monoxide (6.4), methane (24.7), propene (4.9), and 2-methylpropene (62.0). The yield of 2-methylpropene is 22.9%. The results suggest the cyclization of the 2-oxo-3-methyl-1,3-butadiyl diradical (12) to 2,2-dimethylcyclopropanone (13), and subsequent decarbonylation to 2-

(11) The elimination of a methoxy radical could also take place from the 3-chloro-2,2-dimethoxypropyl radical.
(12) S. M. McElvain and P. L. Weyna, *J. Am. Chem. Soc.*, 81, 2579 (1959).

methylpropene (14). The reaction was also conducted at 115–125°, but 2-methylpropene was obtained in a yield of only 1%. The concentration of potassium

vapor is insufficient for complete dehalogenation at this temperature.

3-Oxo-2,4-pentadiyl

The 3-oxo-2,4-pentadiyl diradical (16), formed by the reaction of a mixture of *meso-* and *dl-*2,4-dibromo-3-pentanone (15) with potassium vapor, cyclizes to 2,3-dimethylcyclopropanone (17). Elimination of carbon monoxide from the cyclopropanone 17 results in the isolation of *cis-* and *trans-*2-butene (18) in yields of 11.5 and 15.1%, respectively. The mole ratios of the major products obtained from this reaction at 224–257° are:

*cis-*2-butene (11.7), *trans-*2-butene (15.4), ethene (1.8), ethane (13.3), methane (47.5), and carbon monoxide (7.4). The reaction was also carried out (180–190°) using one of the pure isomers (the *meso* or the *dl*). The same products were produced as were obtained from the mixture of isomers; the yields of *cis-* and *trans-*2-butene were 0.33 and 0.34%, respectively. The isolation of both 2-butenes indicates the absence of stereochemical control in the steps leading to ring closure.

3-Oxo-2,4-dimethyl-2,4-pentadiyl

2,4-Dibromo-2,4-dimethyl-3-pentanone (19) reacts with potassium vapor at 277–297° to give 2,3-dimethyl-2-butene (22), the same product observed in the photolysis of tetramethyl-1,3-cyclobutanedione.[4b] This indicates that the 3-oxo-2,4-dimethyl-2,4-pentadiyl diradical (20) cyclizes to tetramethylcyclopropanone (21). The mole ratios of the products of this reaction are: 2,3-dimethyl-2-butene (18.8), 2,3-dimethyl-1-butene (1.9), 2-methylpropene (1.6), propene (4.6), propane

(3.1), ethane (1.2), and methane (69.4). The yield of C_6 olefin is 11.6%.

2-Oxo-1,3-cycloheptadiyl

The isolation of carbon monoxide and cyclohexene (26) from the reaction of 2,7-dibromocycloheptanone (23) with potassium vapor suggests that the resulting 2-oxo-1,3-cycloheptadiyl diradical (24) closes to give bicyclo[4.1.0]heptan-7-one (25). The products of this reaction effected at 255–265° are cyclohexene (47.1),
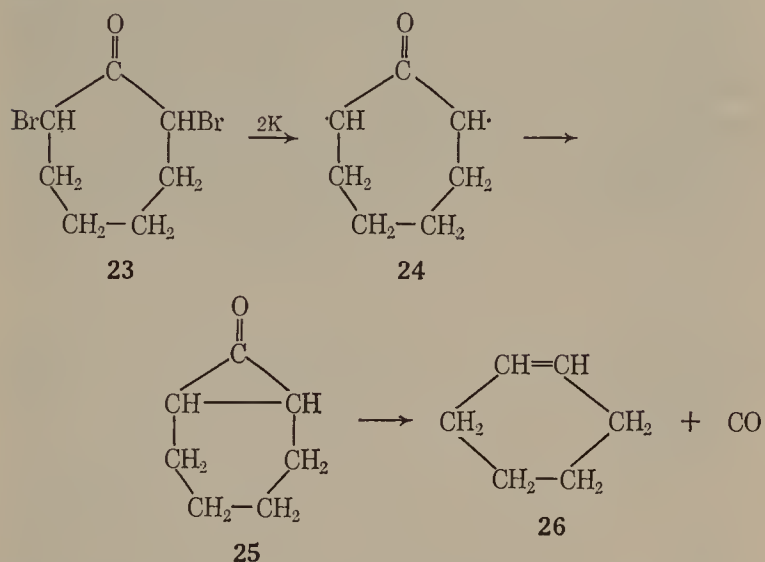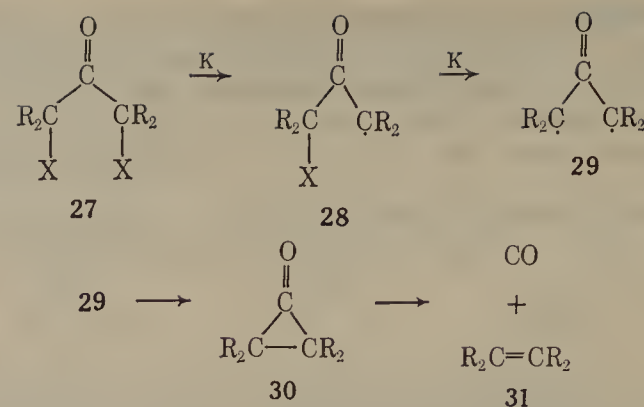

benzene (12.1), propane (2.1), propene (1.2), ethane (3.2), ethene (0.2), methane (11.0), and carbon monoxide (22.3). The combined yields of cyclohexene and benzene are 22.0%. Benzene is probably formed by the dehydrogenation of cyclohexene by potassium. The conversion of 1,4-dimethylenecyclohexane to p-xylene under similar conditions has been reported.[13]

Conclusions

The 2-oxo-1,3-alkadiyl diradicals (29), formed by the reaction of α,α'-dihalo ketones 27 with potassium vapor, cyclize to the cyclopropanones 30. The resulting cyclopropanones eliminate carbon monoxide to give the olefins 31 as the major products.

The steps leading to the cyclopropanone are exothermic, producing a cyclopropanone "hot" by 40–50 kcal. The exothermicity is not readily calculated, but can be estimated as follows. The halo radical 28 would be collisionally quenched by helium atoms, so that its energy is that of the delocalized ($\sim$7 kcal/mole[14a]) ground state. The conversion of 28 to 29 is exothermic, and a substantial part of this exothermicity could be left

(13) R. G. Doerr and P. S. Skell, J. Am. Chem. Soc., 89, 3062 (1967).
(14) (a) P. Nangia and S. W. Benson, ibid., 84, 3411 (1962); (b) J. P. Chesick, ibid., 85, 2720 (1963).

in 29 since the additional stabilization energy of 29 could not be generated until there had been extensive C–X stretching and KX formation. Thus 29 would be "hot," being stabilized only by the original delocalization energy of 28. If ring closure (47–57 kcal/mole[14b]) to 30 is fast compared to collisional deactivation by helium, 30 would be hot by approximately 40–50 kcal. The decompositions of cyclopropanones to carbon monoxide and olefins (30 → 31) are exothermic by about 56 kcal/mole, and could easily have an energy of activation less than 40–50 kcal/mole. If this were the case, the primary product from the ring closure, the "hot" cyclopropanone, would have an energy in excess of that needed for the elimination of carbon monoxide, and thus would not be likely to survive long enough for collisional deactivation. This possibility coupled with the demonstrable high reactivity of ketones with NaK (vide infra), and the high temperature of the reaction zone precluded the isolation of cyclopropanones in this system.

The behavior of the 2-oxo-1,3-propadiyl diradicals should be contrasted to that of their carbon analog, trimethylenemethane (2-methylene-1,3-propadiyl), which was generated under similar conditions.[13] While cyclization to cyclopropanone is the predominant reaction of 2-oxo-1,3-propadiyl, dimerization to 1,4-dimethylenecyclohexane is a predominant reaction of trimethylenemethane. The difference in the behavior of the two species is attributed to a difference in electronic states. From spin considerations a singlet species should cyclize to the three-membered ring and a triplet species should not, giving it a longer lifetime and thus favoring dimerization. On this basis alone the 2-oxo-1,3-propadiyl diradicals generated in this system can be assigned to singlet states and trimethylenemethane to triplet. Molecular orbital calculations[3c,15] predict a triplet ground state for trimethylenemethane and a singlet ground state for 2-oxo-1,3-propadiyl.

The formation of cyclopropanones by the cyclization of the 2-oxo-1,3-alkadiyl diradicals indicates that it reacts from the singlet state. However the law of conservation of spin angular momentum predicts that the reaction between the intermediate halo radical (such as 2) and a potassium atom should give a 3:1 ratio of triplet to singlet 2-oxo-1,3-propadiyl if the E_{act} for 28 → 29 is the same, without regard for multiplicity. The triplet state could decay to the singlet state by collision with a potassium atom, or could react to give other products. Since the yield of olefin 31 is usually about 25%, it is intriguing to speculate that the singlet is con-

(15) A. Streitwieser, Jr., "Molecular Orbital Theory for Organic Chemists," John Wiley and Sons, Inc., New York, N. Y., 1961, Chapters 2, 5.

verted to cyclopropanones, and the triplet is converted to fragmentation or nonvolatile products, perhaps by reaction with potassium forming a potassium dienolate (33).
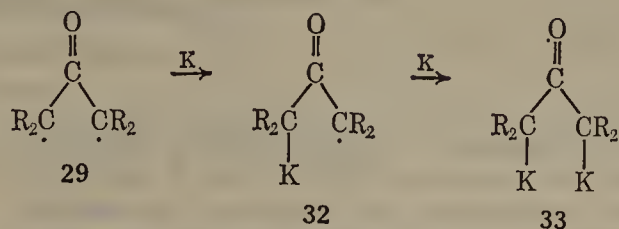
Reaction of Ketones with Potassium Vapor

Simple ketones do not survive the conditions of the reaction system. The reaction of acetone (0.046 mole) with potassium vapor at 278–298° resulted in complete conversion of the acetone, the only products isolated being methane (0.0308 mole) and 2-methylpropene (0.00104 mole). These products account for 48% of the hydrogen and 25% of the carbon of the acetone. Since the pyrolysis of acetone proceeds only slowly at 500°,[16] the products must be formed by reaction with potassium vapor.

Subjecting 2,4-dimethyl-3-pentanone to the reaction conditions at 248–258° led to the recovery of 2% of the starting ketone. The reaction products, obtained in 2.6% yield, consisted primarily of propane and propene. At 170–182°, 2-butanone is recovered in 43% yield. The products, which accounted for only 0.19% of the consumed 2-butanone, were predominantly ethane, ethene, and ethyne.

At higher temperatures ketones are completely converted while at lower temperatures a portion of ketone survives the reaction conditions. The conversion of the ketone to volatile products can be explained either by a thermolysis of an intermediate potassium ketyl or by a catalyzed pyrolysis of the ketone. The catalysis would probably involve the abstraction of hydrogen by potassium atoms, similar to that observed in the iodine-catalyzed pyrolysis of acetone.[17] The nonvolatile products which are predominant at lower temperatures are most likely formed from the potassium ketyl.

Experimental Section

1,3-Dibromo-3-methyl-2-butanone, bp 98–100° (18 mm), was prepared by the method of Favorsky and Wanscheidt, bp 99° (18 mm).[18] The compound was redistilled before use, bp 87° (10 mm), $n^{25}D$ 1.5162. The nmr spectrum consisted of two singlets at 1.95 and 4.37 ppm (δ scale) in a respective ratio of 3:1.

Preparation of 2,4-Dibromo-3-pentanone. A mixture of 3-pentanone (53 ml, 43 g, 0.50 mole), glacial acetic acid (50 ml), and water (50 ml) was placed in a 300-ml flask fitted with a mechanical stirrer, a reflux condenser, and a dropping funnel. Bromine (160 g, 1.00 mole) was added dropwise to the solution maintained at 25°. After the addition of bromine, the mixture was washed with water and dried over calcium chloride.

The liquid was then distilled on a 10-cm Vigreux column. A total of 102 g (84% yield) of product, bp 67–82° (10 mm), was obtained [bp 65–70 (8 mm)].[19] A center fraction, bp 75–78° (10 mm), gave an nmr spectrum which showed two doublets at 1.79 and 1.87 ppm and two quartets centered at 4.78 and 4.97 ppm, indicating that the fraction consisted of a mixture of *meso* and *dl* forms of the symmetrical dibromo ketone. The lower boiling isomer was separated by distillation through a 30-cm Vigreux column, bp 69–71° (10 mm). The nmr spectrum of this fraction showed that it was the isomer with the peaks at 1.79 and 4.97 ppm.

Preparation of 2,4-Dibromo-2,4-dimethyl-3-pentanone. Bromine (160 g, 1.00 mole) was added dropwise to 2,4-dimethyl-3-pentanone (58 g, 0.50 mole) contained in a 250-ml, three-necked flask, fitted with a stirrer, reflux condenser, and dropping funnel. At 0°, bromine color was discharged rapidly until half of the bromine was added. Phosphorus tribromide (1 ml) was added as a catalyst, and the reaction mixture was heated overnight on a steam bath. Helium was swept through the solution to displace hydrogen bromide; the solution was dried over calcium chloride and distilled through a 30-cm Vigreux column to give 2,4-dibromo-2,4-dimethyl-3-pentanone, 85.6 g (62% yield); bp 87–89° (10 mm) [bp 84–85° (9 mm)[20], $n^{25}D$ 1.5026. The nmr spectrum consisted of a singlet at 2.14 ppm.

Preparation of 2,7-Dibromocycloheptanone. Bromine (80 g, 0.50 mole) was added dropwise to a 25° mixture of cycloheptanone (28 g, 0.25 mole), acetic acid (25 ml), and water (25 ml). After 2 hr, dilution with water separated a semisolid. The crude product (57 g, 85% yield) was recrystallized from methanol and from pentane to give white crystals (31.0 g, 46% yield), mp 65–66° (mp 68–69° [21]).

1,3-Dichloro-2,2-dimethoxycyclopropane, mp 82°, was prepared by the method of Pryanishnikov and Leontowitsch,[22] who reported a melting point of 81.5°.

Reaction with Alkali Metal Vapor. The reactant was added slowly to the heated vaporization coil of the previously described apparatus,[9] while helium (300 mm) was passed through the coil at a flow of 1.0 l./min (STP). The helium stream, containing 5–25 mm partial pressure of the reactant, was passed through a fine spray of heated sodium–potassium alloy (78 wt % potassium) which kept the helium saturated with alkali metal vapor.

The products of the reaction were collected in two −196° traps packed with glass wool and a −196° trap packed with silica gel. The fractions were analyzed by vapor phase chromatography and the individual components identified by comparison of their infrared spectra and vpc retention times with those of the known compounds. Corrections were made for thermal conductivity differences of the components.

Preparation of 2-Methoxypropene. Iodine (57 g, 0.23 mole) was added over a period of 0.5 hr to a stirred mixture of propene (10 g, 0.42 mole), HgO (37.2 g, 0.152 mole), and methanol (100 ml) at −78°. The mixture was allowed to warm to room temperature while stirring. It was filtered, and the filtrate was poured into 300 ml of water. The lower layer was separated, added to a flask containing KOH (15 g, 0.27 mole) in methanol (50 ml), and refluxed for 3 hr. Distillation of the reaction mixture separated 2-methoxypropene, 5.5 g (34% yield), bp 34–36° (bp 33.5° [23]).

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Trimethylenemethane[1]

Philip S. Skell and Robert G. Doerr

Contribution from the Department of Chemistry, The Pennsylvania State University, University Park, Pennsylvania 16802. Received April 10, 1967

Abstract: Trimethylenemethane (II) was prepared by the reaction of 2-halomethyl-3-halopropene (I) with potassium vapor. The products of this reaction consisted of 1,4-dimethylenecyclohexane (III), *p*-xylene, 2-methylpropene (IV), methylenecyclopropane, and the normal butenes. These results suggest the intermediacy of trimethylenemethane existing in the triplet state. 1,4-Dimethylenecyclohexane is formed by the dimerization of two triplet molecules with opposite spins, and 2-methylpropene is formed by the abstraction of two hydrogen atoms. The three butenes are produced, at least in part, by a secondary reaction of potassium vapor with methylenecyclopropane. In contrast, the saturated 1,3-diradical VI, formed in the reaction of 1,3-diiodo-2-methylpropane (V) with potassium vapor, gives methylcyclopropane and 2-methylpropene. 1,4-Dimethylcyclohexane or other products due to dimerization were not detected. Trimethylenemethane does not react with ethene, but does react with other triplet molecules. The generation of triplet methylene in the presence of trimethylenemethane leads to methylenecyclobutane and 2-methyl-1-butene.

Trimethylenemethane (II) has been the subject of considerable theoretical discussion. Molecular orbital calculations[2] predict that trimethylenemethane will have a triplet ground state and a delocalization energy of 1.46β ($\sim$34 kcal) relative to the classical structure of one double bond and two localized electrons. The complete configuration interaction treatment of trimethylenemethane also predicts a triplet ground state.[3] The sum of the bond orders at the central carbon is 4.732. This is the maximum value for the sum of the bond orders at a carbon atom,[4] and is used as a reference for the calculation of free valence indices.[5] This molecule has been used as a model for the calculation of negative spin densities in triplet molecules[6] and for the calculation of the energy involved in the formation of a diradical isomer of cyclopropanone.[7]

Trimethylenemethane has recently been prepared by matrix photolysis of 4-methylene-1-pyrazoline at $-185°$[8a] and of 3-methylenecyclobutanone at $-196°$.[8b] The esr spectrum confirmed that trimethylenemethane was a symmetrical ground-state triplet.[8] Pyrolysis of 4-methylene-1-pyrazoline resulted in its conversion to methylenecyclopropane.[9] Deuterium labeling showed that the original methylene group in the pyrazoline was at least partially equilibrated with the methylene groups in the cyclopropane ring. The results were explained by the formation of a symmetrical intermediate in which dideuteriomethylene groups were slower to rotate into position for ring closure than were diprotiomethylene groups. A similar equilibration was observed in the formation of alkylidenecyclopropanes from the photolysis of 4-alkylidene-1-pyrazolines.[10] The extent of equilibration was greatly increased when the photolysis was photosensitized with benzophenone or triphenylene.[10b] The authors suggested that the photosensitized photolysis led to the triplet state of the trimethylenemethane derivative and direct photolysis involved the singlet state.

Derivatives of trimethylenemethane have been postulated as intermediates in the rearrangement of substituted methylenecyclopropanes.[11] On the basis of stereochemical evidence, Ullman[11c] concluded that the rearrangement of the dimethyl ester of Feist's acid proceeded through both a symmetrical intermediate and a "valence tautomerization" involving simultaneous cleavage and re-formation of the cyclopropyl ring bonds.

Trimethylenemethaneiron tricarbonyl, an organometallic complex of this intermediate, was prepared.[12]

The reaction of alkali metal vapor with organic halogen compounds is a method for generating mono- and diradical species. This reaction has been studied extensively from a kinetic viewpoint.[13] For example, the reaction between sodium atoms and methyl iodide, methyl bromide, or methyl chloride occurs with 1, 50, and 10,000 respective collisions. Passage of the organic species formed by the reaction of methyl bromide and sodium vapor into a vessel of iodine vapor produces methyl iodide.[14] The same species removes mirrors of antimony and tellurium, in the latter case forming dimethyl ditelluride.[15] Product analysis also supports the formation of methyl and ethyl radicals,[16-18] the vinyl radical,[19,20] and halomethyl radicals.[21-24] Sim-

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ilarly, the reaction of dihaloalkanes with alkali metal vapor produces organic diradicals.[25-30] For example, 1,3-dihalopropane gives the 1,3-diradical which cyclizes to cyclopropane or rearranges to propene.[25-26]

Trimethylenemethane

Trimethylenemethane was prepared by the reaction of potassium vapor[31] with 2-iodomethyl-3-iodopropene. The products from this reaction carried out at different temperatures are given in Table I.

Table I. Reaction of 2-Iodomethyl-3-iodopropene with NaK

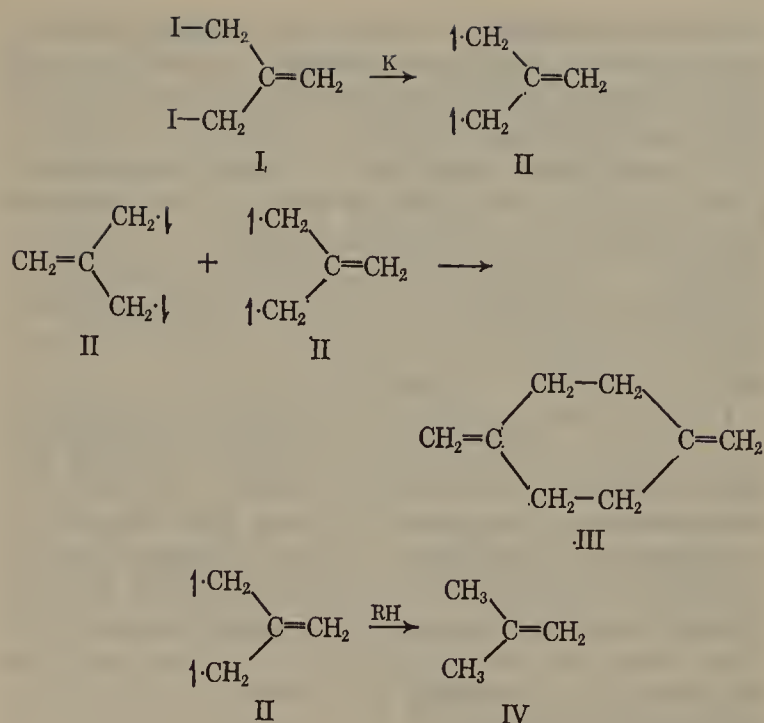|	Reaction			
	1	2	3	4[a]
	Temp, °C			
	228–235	232–236	247–267	226–232
Products	Mole % yield			
2-Methylpropene	14.0	13.3	13.0	13.5
1-Butene	2.2	2.7	2.2	4.3
trans-2-Butene	8.1	5.8	4.4	5.8
cis-2-Butene	5.3	4.7	3.5	3.7
Methylenecyclopropane	0	0	0.8	0
1,4-Dimethylenecyclohexane	1.3	11.0	11.3	14.0
p-Xylene	33.5	22.3	16.0	14.0
Total	64.3	59.8	51.2	55.8

[a] Conducted in the presence of a 20-fold excess of ethene.

The formation of 1,4-dimethylenecyclohexane and 2-methylpropene suggests the intermediacy of trimethylenemethane existing in the triplet state. 1,4-Dimethylenecyclohexane would be formed by the dimerization of two triplet molecules of trimethylenemethane with opposite spins, and 2-methylpropene by the abstraction of two hydrogen atoms from neighboring hydrocarbon or potassium hydride.
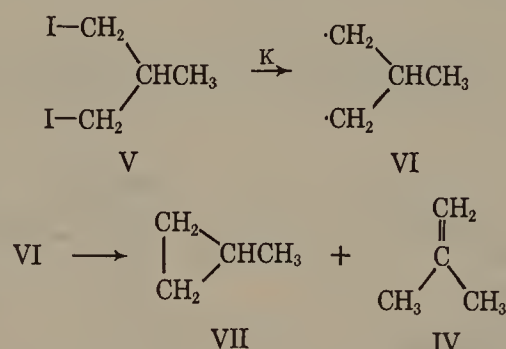
The formation of p-xylene is due to a secondary reaction of 1,4-dimethylenecyclohexane. The sum of the yields of the two compounds remains constant at similar temperatures (i.e., 34.7% in reaction 1 and 33.3% in reaction 2), while the ratio of the two is variable. The dehydrogenation of cyclohexene to benzene under similar conditions has been reported.[30]

To determine whether any of the above products could arise from a thermal reaction of 2-iodomethyl-3-iodopropene, a sample of the diiodide was decomposed at 210°. The pyrolysis produced only iodine and a black polymeric material.

The reactions of trimethylenemethane (II) and 2-methyl-1,3-propadiyl (VI), the diradical formed from

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(31) The predominant reacting species in the previously described sodium–potassium alloy (NaK) spray apparatus would be monatomic potassium: P. S. Skell, E. J. Goldstein, R. J. Petersen, and G. L. Tingey, Chem. Ber., 100, 1442 (1967).

the saturated diiodide V, are different. Reaction of 1,3-diiodo-2-methylpropane (V) with potassium vapor at 227–228° results in the formation of methylcyclopropane (VII), 2-methylpropene (IV), 2-methylpropane, and 1-butene in yields of 76.7, 3.3, 0.2, and 0.3%, respectively. 1,4-Dimethylcyclohexane or other prod-

ucts due to dimerization were not detected. Extensive studies of 1,2-, 1,3-, 1,4-, and 1,5-diradicals testify to the insignificance of dimerization in the reactions of saturated diradicals generated from dihalides in this system.[26,28] Dimerization products were not formed by pyrolysis of 1-pyrazolines.[32]

While reaction of potassium vapor with 1,3-diiodo-2-methylpropane would give both the singlet and triplet 1,3-diradicals, the formation of methylcyclopropane and 2-methylpropene would take place only from the singlet. Ring closure of the triplet to triplet cyclopropane (conservation of spin multiplicity) and hydrogen migration in the triplet 1,3-diradical to form triplet 2-methylpropene are endothermic processes, the latter by about 14 kcal/mole.[29] The triplet 1,3-diradical can easily be converted to the singlet state (or to singlet cyclopropane or 2-methylpropene) by collision with a doublet potassium atom.

The unusual behavior of trimethylenemethane compared to other 1,3-diradicals can be explained by the large delocalization energy of the triplet ground state which makes it the favored state under either thermodynamic or kinetic control. Cyclization of triplet trimethylenemethane to triplet methylenecyclopropane is endothermic by about 25–50 kcal/mole. If cycliza-

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tion of triplet trimethylenemethane to singlet methylene-cyclopropane (~20 kcal exothermic) were not strongly spin forbidden, trimethylenemethane would not survive in solid matrices at −185°.[8] Thus since no favorable unimolecular path is available, trimethylene-methane accumulates until its concentration becomes high enough for bimolecular coupling to become a dominant reaction. Hydrogenation to 2-methylpro-pene is also favored by the long life of the trimethylene-methane triplet. The analogous reactions are minor with the saturated 1,3-diradicals.

Trimethylenemethane was generated in the presence of a 20-fold excess of ethene to determine whether this intermediate would react with olefins. The results of the reactions are presented in column 4 of Table I. A comparison of these results to those obtained from the reaction of 2-iodomethyl-3-iodopropene in the absence of ethene show that trimethylenemethane does not react with ethene and that the presence of ethene has little effect on the distribution of products obtained from trimethylenemethane.

Two reactions in which the precursor of trimethylene-methane was changed from a diiodide to a dichloride were carried out. The results of the reactions of 2-chloromethyl-3-chloropropene with potassium vapor are recorded in Table II.

Table II. Reaction of 2-Chloromethyl-3-chloropropene with NaK

	Reaction	
	1	2
	Temp, °C	
	237–243	270
Products	Mole % yield	
Methane	0.5	1.5
Ethane	0.8	3.4
Ethene	0.9	1.4
2-Methylpropene	9.7	12.4
1-Butene	5.2	5.7
trans-2-Butene	4.7	8.0
cis-2-Butene	5.7	5.9
Methylenecyclopropane	5.2	0
Benzene	0.5	0
1,4-Dimethylenecyclohexane	5.9	2.1
p-Xylene	3.0	4.7
Total	41.1	43.1

The same products are observed as appeared in the reaction of the diiodide, but the yields of 2-methylpro-pene and especially the dimerization products have been reduced. The differences in the reactions of the diiodide and the dichloride can be explained by the greater reactivity of alkyl iodides.

Methyl iodide has been reported to require an average of only one collision with a sodium atom for reaction.[13] Since the diiodide in question is an allyl iodide, it would be expected to be equally reactive. Allyl chloride has a reactivity about 0.005 times that of methyl iodide, and saturated primary alkyl chlorides are ~10⁻⁴ times as reactive as methyl iodide.[13] It would then be expected that after one halogen had been removed from 2-halomethyl-3-halopropene, the remaining chloro radical would have a lifetime at least 200 times that of the corresponding iodo radical. Thus the buildup of trimethylenemethane concentration required for di-

merization would not be as great as with the diiodide, and reactions with first-order involvement of trimethylene-methane are preferred.

The sum of the yields of the normal butenes and methylenecyclopropane remains reasonably constant. This fact suggests that the formation of the butenes may be due to a secondary reaction of methylenecyclo-propane. To test this hypothesis, a sample of methyl-enecyclopropane was subjected to the reaction condi-tions. Only 7% of the methylenecyclopropane was recovered and a mixture of the normal butenes was pro-duced in good yield.

The apparent formation of singlet methylenecyclo-propane from a triplet intermediate deserves some com-ment. The law of conservation of spin angular mo-mentum predicts that the encounters between the inter-mediate iodo radical and potassium atoms should lead to triplet combinations three times as frequently as singlet. The elimination of potassium iodide from either of these collision complexes is probably high since alkyl iodides react at nearly every collision. Thus a 3:1 ratio of triplet to singlet trimethylenemethane is pre-dicted. Singlet trimethylenemethane could either form methylenecyclopropane or decay to the triplet state. Conversion of triplet trimethylenemethane to singlet is improbable on energetic grounds, but three out of four collisions with potassium atoms could lead directly, by an energetically favorable route, to singlet methylene-cyclopropane and potassium atoms with inverted spin designations.

Reaction of Triplet Methylene and Allene

An attempt was made to produce trimethylenemeth-ane by the reaction of dibromomethane with potassium vapor in the presence of allene. It has been reported that dibromomethane reacts with potassium to give triplet methylene.[29] Triplet methylene could add to the center carbon of allene, as do methyl radicals,[33] to give a triplet intermediate which upon rotation about the carbon–carbon single bond would give planar tri-methylenemethane.

The experiment was conducted at 205–230° using 0.051 mole of dibromomethane and 0.35 mole of al-lene. The products obtained from the reaction of triplet methylene and allene consisted of 1-butene (8.4% yield) and methylenecyclopropane (11.3% yield). Products expected for the intermediacy of trimethylene-methane were not detected. At 270–280° the products (and their yields) were butane (0.6%), 1-butene (2.4%), cis-2-butene (1.3%), trans-2-butene (1.2%), and 2-methylpropene (0.6%). Again the dimerization prod-ucts of trimethylenemethane were absent.

The failure to produce trimethylenemethane can be explained in two ways. The first is the sensitivity of allene to the reaction conditions. Allene is efficiently converted to nonvolatile products and, in low yield, to a mixture of propane and propene. The second is the possibility that triplet methylene does not add to the center carbon of allene but, like the trifluoromethyl radical,[34] adds to the terminal carbon.

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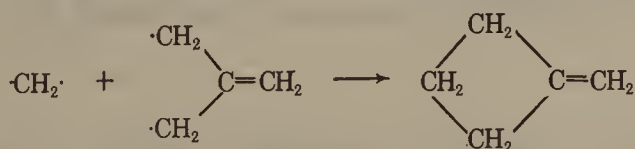## Reaction of Triplet Methylene and Trimethylenemethane

Since trimethylenemethane appears to be a triplet species that dimerizes, addition of another triplet intermediate should be the most effective means of trapping trimethylenemethane. Diiodomethane should yield triplet methylene as does dibromomethane. Simultaneous reaction of 2-iodomethyl-3-iodopropene and a fivefold excess of diiodomethane with potassium vapor was effected at 235–240°. The results are given in Table III. In addition to the usual products from

Table III. Reaction of 2-Iodomethyl-3-iodopropene with Excess Diiodomethane and NaK

Products	Mole % yield
2-Methylpropane	0.3
2-Methylpropene	10.4
Butane	1.2
1-Butene	7.2
trans-2-Butene	8.6
cis-2-Butene	6.2
1,3-Butadiene	0.1
2-Methyl-1-butene	1.5
2-Methyl-2-butene	1.3
3-Methyl-1-butene	0.1
Methylenecyclobutane	1.4
1-Methylcyclobutene	0.6
Pentane	0.1
1-Pentene	0.1
trans-2-Pentene	0.2
Benzene	0.5
1,4-Dimethylenecyclohexane	6.3
p-Xylene	10.4
Unidentified liquids (largest component is 1.4%)	6.8
Total	63.3

trimethylenemethane, a number of C_5 olefins were obtained, indicating a reaction of trimethylenemethane with methylene.

The products can be rationalized by the formation of a vibrationally excited methylenecyclobutane (~100 kcal exothermic) which is partially quenched, the remainder isomerizing to 1-methylcyclobutene and the open-chain dienes, 2-methyl-1,3-butadiene and 1,3-pentadiene. Under the reaction conditions the con-

jugated dienes are expected to be hydrogenated to the C_5 olefins. At 180° 1,3-butadiene is converted in 47% yield as a mixture of butane and the butenes, the remainder being nonvolatile material.[28]

Trimethylenemethane is effectively trapped with triplet cyclobutadienes.[1a,b] The details of these reactions will be presented later.

Experimental Section

Preparation of 2-Chloromethyl-3-chloropropene. 2-Methyl-3-chloropropene (272 g, 3.00 moles) was chlorinated[36] until the refractive index (n^{25}D) was 1.4775. The mixture was washed with water and dried over anhydrous Na_2SO_4. Analysis by vpc (Carbowax,

74°) showed that the mixture consisted of 2-chloromethyl-1-chloropropene (30 and 9%, probably cis and trans), 2-chloromethyl-3-chloropropene (31%), and 2-methyl-1,2,3-trichloropropane (30%).

The mixture was distilled on a spinning-band column, following the progress of the distillation by vpc. A 10-g sample of 2-chloromethyl-3-chloropropene was obtained, bp 60° (50 mm) [58° (50 mm)[35a]], which was greater than 99% pure. The nmr spectrum consisted of two singlets at 4.19 and 5.32 ppm (δ scale) in a ratio of 2:1. The nmr of a 2-chloromethyl-1-chloropropene fraction, bp 54–55° (50 mm) [lit.[35a] bp 54° (50 mm)], showed a fine doublet at 1.90 ppm, a singlet at 4.21 ppm, and a multiplet at 5.97 ppm in a ratio of 3:2:1. The nmr spectrum of 2-methyl-1,2,3-trichloropropane, bp 80° (50 mm) [bp 74° (45 mm)[35b]], consisted of two singlets at 1.73 and 3.89 ppm in a ratio of 3:4.

Preparation of 2-Iodomethyl-3-iodopropene. A mixture (24 g, 0.19 mole) consisting of 25% 2-chloromethyl-3-chloropropene and 75% 2-chloromethyl-1-chloropropene was added to KI (63 g, 0.38 mole) in 400 ml of acetone. A precipitate formed immediately. The mixture was refluxed 8 hr. It was filtered and concentrated to 100 ml by distillation. The concentrate was poured into 300 ml of water and extracted with 100 ml of pentane. The pentane solution was washed with $Na_2S_2O_3$ solution and water and dried over anhydrous Na_2SO_4.

The pentane was removed by distillation and the product was distilled (5 mm) through a 10-cm Vigreux column. Two products were obtained: 2-iodomethyl-1-chloropropene (22.5 g, 0.104 mole, 73%; bp 49–52°) and 2-iodomethyl-3-iodopropene (9.6 g, 0.031 mole, 65%; bp 83–85°).

2-Iodomethyl-3-iodopropene crystallized on cooling. The solid was washed with $Na_2S_2O_3$ and recrystallized from hexane at reduced temperature to give white plates, mp 32–33°.

Reaction of 2-Iodomethyl-3-iodopropene with NaK. 2-Iodomethyl-3-iodopropene (2.8 g, 0.0091 mole) was placed in the vaporization coil of the NaK apparatus.[31] The atmosphere inside the apparatus was maintained at 200-mm helium pressure. Helium flowed through the vaporization coil (2.0 l./min, STP), carrying the diiodide through a preheater into the reaction zone. Simultaneously, a fine spray of NaK (88 wt % K) saturated the helium in the reaction zone with potassium vapor. The helium stream containing the products was passed successively through two traps packed with glass wool and a trap packed with silica gel, all at −196°. The temperature of the vaporization coil was 60°, and the temperature of the reaction zone varied between 232 and 236° during the 18-min reaction.

Analysis of the material in the −196° silica gel trap by infrared spectroscopy and vpc (molecular sieve, 25°) showed that only air had been trapped. The products in the two −196° traps packed with glass wool were distilled through a −78° trap into a −196° trap on the vacuum line.

A liquid remained in the −78° trap which weighed 0.16 g. Analysis by vpc (Carbowax 1000, 100°; and dipropylene glycol dibenzoate, 115°) showed that the liquid consisted of two components. The components were collected individually and identified as 1,4-dimethylenecyclohexane, 33.2%, and p-xylene, 66.8%, on the basis of the following evidence. The mass spectrum of p-xylene has a parent peak at m/e 106, corresponding to C_8H_{10}. The nmr spectrum consisted of two singlets at 2.27 and 6.93 ppm in a ratio of 3:2. The infrared spectrum was identical with that of the known compound. The mass spectrum of 1,4-dimethylenecyclohexane had a parent peak at m/e 108, corresponding to C_8H_{12}. The nmr showed two singlets at 2.20 and 4.64 ppm in a ratio of 2:1. The infrared spectrum was identical with that given in the literature.[36] 1,4-Bis(bromomethyl)-1,4-dibromocyclohexane, mp 132–134° (134–135°[36]), a known derivative of 1,4-dimethylenecyclohexane, was obtained by reaction with bromine in ether at −20°.

The gas in the −196° trap on the vacuum line (0.00247 mole) was analyzed by vpc (2,5-hexanedione, 0°). The products were identified by comparison of their infrared spectra and vpc retention times with those of the known compounds. The infrared spectrum of methylenecyclopropane was identical with that in the literature.[21] Relative response corrections were made for differences in thermal conductivity.

The complete results of this reaction are given in column two of Table I. The results of two similar reactions at different temperatures are given in columns one and three of Table I. The reactions using 2-chloromethyl-3-chloropropene were conducted in a

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(36) F. Lautenschlaeger and G. F. Wright, Can. J. Chem., 41, 1972 (1963).

similar manner, except that the dichloride was added dropwise into the vaporization coil.

Pyrolysis of 2-Iodomethyl-3-iodopropene. 2-Iodomethyl-3-iodopropene (2 g) was placed in a 25-ml distilling flask, and the flask was heated to 210°. Nothing volatile were observed. Iodine and a black polymeric material remained in the flask.

Reaction of 2-Iodomethyl-3-iodopropene with NaK in the Presence of Ethene. The reaction was carried out as above (3.1 g, 0.010 mole of 2-iodomethyl-3-iodopropene) except that ethene (0.20 mole) was added to the helium stream over the duration of the 18-min reaction period. Analysis of products was the same as above.

Preparation of 1,3-Diiodo-2-methylpropane. Attempts to prepare this compound by the Finkelstein exchange from 1-bromo-3-chloro-2-methylpropane under the usual conditions of refluxing acetone or 2-butanone resulted in replacement of the bromine alone. 1-Iodo-3-chloro-2-methylpropane, bp 45–47° (5 mm), was obtained in 74% yield. The mass spectrum had a parent peak at m/e 218. The nmr spectrum consisted of doublets at 1.12, 3.30, and 3.54 ppm, and a multiplet at 1.83 ppm in a ratio of 3:2:2:1.

The diiodide was obtained in 20% yield by carrying out the exchange reaction in a 100° acetone solution for 68 hr, employing a high-pressure bomb. The pure diiodide was isolated by distillation, bp 56–57° (1 mm). The nmr spectrum showed two doublets at 1.16 and 3.27 ppm, and a multiplet at 1.60 ppm in a ratio of 3:4:1.

Reaction of 1,3-Diiodo-2-methylpropane. The diiodide (2.47 g, 0.00797 mole) was vaporized from the 95° coil over a period of 12 min and was carried into the 227–228° reaction zone. The products were distilled through a −78° trap into a −196° trap on a vacuum line. Nothing was collected in the −78° trap. The gas in the −196° trap (0.00640 mole, 80.3% yield) was analyzed by vpc.

Simultaneous Reaction of Allene and Dibromomethane with NaK. Dibromomethane (8.8 g, 0.051 mole) was added dropwise to the vaporization coil of the NaK apparatus, and allene (0.34 mole) was added simultaneously to the helium carrier stream. The temperature of the vaporization coil was 74° and that of the reaction zone varied between 200 and 230°. The reaction time was 25 min.

The product was distilled through a −78° trap into a −196° trap on the vacuum line. The product in the −78° trap (0.1 g) consisted of six unidentified liquids with retention times less than those of 1,4-dimethylenecyclohexane and p-xylene. The gas in the −196° trap (0.125 mole) consisted of (mole ratios) propane (5), propene (55), allene (33), 1-butene (3), and methylenecyclopropane (4). From a reaction at 270–280° none of the allene was recovered.

Reaction of 2-Iodomethyl-3-iodopropene with Excess Diiodomethane and NaK. 2-Iodomethyl-3-iodopropene (2.7 g, 0.0087 mole) and diiodomethane (12.2 g, 0.046 mole) were mixed and added dropwise to the vaporization coil of the NaK apparatus. The temperature of the vaporization coil was 100° and that of the reaction zone varied between 235 and 240°. The reaction was conducted over a period of 20 min.

The product was distilled through a −78° trap into a −196° trap on the vacuum line. A liquid, weighing 0.12 g, remained in the −78° trap. Analysis by vpc (Carbowax, 63°; and dipropylene glycol dibenzoate, 118°) showed that the liquid consisted of (mole ratios) benzene (2), 1,4-dimethylenecyclohexane (20), p-xylene (33), and 17 unidentified components (45). The gas (0.00945 mole) was analyzed by vpc (dipropylene glycol dibenzoate, 25°; and 2,5-hexanedione, 0°). The products probably derived only from CH_2I_2 consisted (mole ratio) of ethane (9.8), ethene (80.0), propane (1.9), propene (6.7), and cyclopropane (1.7), the remainder of the gases being derived from trimethylenemethane (see Table III

Reaction of Triphenylmethyl with Diazomethane

Donald B. Denney and Neil F. Newman

Contribution from the School of Chemistry, Rutgers, The State University, New Brunswick, New Jersey 08903. Received February 25, 1967

Abstract: The reaction of triphenylmethyl with diazomethane has been studied under several sets of conditions. The major products are 1,1,1,3,3,3-hexaphenylpropane, triphenylmethane, triphenylethylene, and 1,1,2-triphenylethane. The yields of products are strongly dependent on the concentration of reactants with the hexaphenylpropane being formed in greatest amount under more concentrated conditions. The results of these experiments are most easily explained by a mechanism which involves formation of a 2,2,2-triphenylethyl radical by reaction of a triphenylmethyl radical with diazomethane. This radical can then rearrange or react with triphenylmethyl to give 1,1,1,3,3,3-hexaphenylpropane. It has been found that this substance decomposes quantitatively at 250° to triphenylmethane and triphenylethylene.

Although diazomethane most commonly reacts by ionic or carbene pathways, it is also susceptible to attack by free radicals. The presence of radical intermediates in diazomethane reactions has been demonstrated by Urry and co-workers[1] who observed a high quantum yield in photoinitiated reactions of diazomethane with polyhalomethanes. They proposed that a radical chain reaction was involved.

More recently Müller and co-workers[2] have investigated the reaction of diazomethane with aryloxy radicals. The products are methylene acetals and these can be most easily explained by a free radical mechanism. These workers also reinvestigated the reaction of triphenylmethyl with diazomethane which was

originally described by Schlenk.[3] Schlenk reported that 1,1,1,3,3,3-hexaphenylpropane (II) was formed as the product of this reaction.

$$(C_6H_5)_3C\cdot + CH_2N_2 \longrightarrow (C_6H_5)_3CCH_2C(C_6H_5)_3 + N_2$$
$$\text{I} \qquad\qquad\qquad \text{II}$$
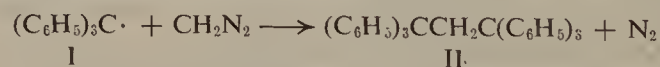
The structural assignment was based on molecular weight and analytical data. Müller, *et al.*, isolated the same compound and reported its nmr spectrum which showed a single absorption at 4.13 ppm and aromatic protons at 6.86 ppm in the ratio of 1:15. This spectrum is certainly in agreement with the structural assignment except perhaps for the position of the –CH₂– absorption which is downfield from the normal region where this is found. This downfield shift could be due to deshielding by the aromatic rings.

(1) W. H. Urry, J. R. Eiszner, and J. W. Wilt, *J. Am. Chem. Soc.*, **79**, 918 (1957).

(2) E. Müller, A. Moosmayer, and A. Rieker, *Z. Naturforsch.*, **186**, 982 (1963).

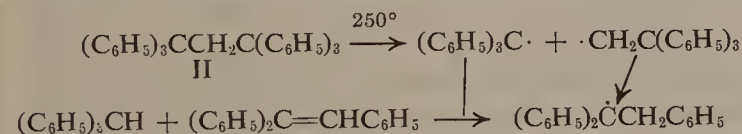(3) W. Schlenk and C. Bornhardt, *Ann.*, **394**, 183 (1912).

These observations are of particular interest because the most reasonable mechanism for the reaction of triphenylmethyl with diazomethane would involve the 2,2,2-triphenylethyl radical as an intermediate. At the time of the inception of this present study all attempts but one to prepare this radical and trap it before it rearranged had been unsuccessful.[4,5] The only indication that a 2,2,2-triphenylethyl radical had any stability arose from the finding of 1,1,1,4,4,4-hexaphenylbutane as a product of the decomposition of 3,3,3-triphenylpropanoyl peroxide.[6] The yield of this material was very small; however, this could have been due to factors other than the instability of the 2,2,2-triphenylethyl radical.

Quite recently Kaplan[7] has studied the reduction of 2,2,2-triphenylethyl chloride by triphenyltin hydride. He has found that 1,1,1-triphenylethane can be obtained in yields as high as 90% by using suitable reaction conditions. He concluded that the 2,2,2-triphenylethyl radical was formed and was efficiently trapped before rearrangement.

It was the purpose of this work to (1) investigate the mechanism of the triphenylmethyl–diazomethane reaction, (2) to add further structural proof for the 1,1,1,-3,3,3-hexaphenylpropane, and (3) if 2,2,2-triphenylethyl radicals were involved to try and learn more about their stability.

Results and Discussion

The reaction of triphenylmethyl with diazomethane in benzene at 25° affords the material reported to be 1,1,1,3,3,3-hexaphenylpropane. Further structural proof for this material has been obtained by studying its thermal decomposition. After 1 hr at 250° complete decomposition had occurred and a quantitative yield of triphenylmethane and triphenylethylene was obtained.

$$(C_6H_5)_3CCH_2C(C_6H_5)_3 \xrightarrow{250°} (C_6H_5)_3C\cdot + \cdot CH_2C(C_6H_5)_3$$
$$\text{II}$$
$$(C_6H_5)_3CH + (C_6H_5)_2C{=}CHC_6H_5 \longrightarrow (C_6H_5)_2\overset{\cdot}{C}CH_2C_6H_5$$

The products of this reaction can be easily rationalized if the starting material is in fact II and thus on this basis and the other evidence the structure seems firmly established.[8]

(4) D. Y. Curtin and M. J. Hurwitz, *J. Am. Chem. Soc.*, **74**, 5381 (1952).
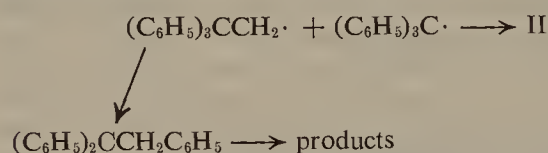(5) D. Y. Curtin and T. C. Miller, *J. Org. Chem.*, **25**, 885 (1960).
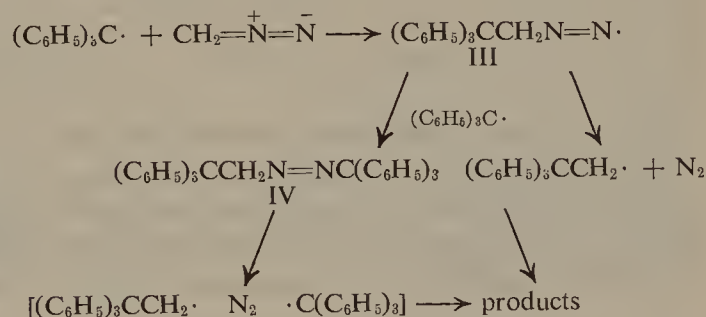(6) D. B. Denney, R. L. Ellsworth, and D. Z. Denney, *J. Am. Chem. Soc.*, **86**, 1116 (1964).
(7) L. Kaplan, *ibid.*, **88**, 4531 (1966).
(8) A referee has suggested that an alternate structure, (C6H5)3C-C(C6H5)2CH2C6H5, should be considered for II. We had considered this as a possibility and discarded it for two reasons. The yield of II varies as a function of the concentration of starting materials. This is what is predicted for II if it is in fact 1,1,1,3,3,3-hexaphenylpropane. If it is 1,1,1,2,2,3-hexaphenylpropane then the yield should not vary as a function of concentration, nor should the relative amounts of products change. There is no report of the preparation of 1,1,1,2,2,3-hexaphenylpropane in the literature; however, one can predict from the stabilities of structurally similar materials that it will be quite unstable. Pentaphenylethane is known to react with oxygen quite rapidly, $t_{1/2} = 49$ min at 80°; see J. Coops, H. Galenkamp, J. Haantjes, H. L. Luirink, and W. Th. Nauta, *Rec. Trav. Chim.*, **67**, 469 (1948), and references therein. K. Ziegler, A. Seib, K. Knovenagel, P. Herte, and F. Andreas, *Ann.*, **551**, 161 (1942), have studied the reactions of various compounds, RC(C6H5)2C(C6H5)2R, with oxygen. They find when R = C2H5, $t_{1/2} = 60$ min, and R = n-C3H7, $t_{1/2} = 1.3$ min at 20°. These data are relevant to our understanding of the influences of resonance and steric effects in promoting the dissociation of the carbon–carbon bond. It is quite apparent that 1,1,1,2,2,3-hexaphenylpropane has the ability to dissociate into a triphenylmethyl radical as does pentaphenylethane,

Investigation of the reaction mixture after the removal of II showed that triphenylmethane, triphenylethylene, and 1,1,2-triphenylethane were also products of the reaction. No evidence for the formation of 1,1,1-triphenylethane was obtained; however, trace amounts (<1–2%) could have escaped detection. The rearranged triphenylethyl compounds are indicative of the formation of a 2,2,2-triphenylethyl species and in this case the radical is by far the most likely candidate.[9] Furthermore it was found that the ratio of rearranged material to II varied as a function of the concentration of starting material. For example, a solution whose initial concentration of hexaphenylethane was 8.5×10^{-2} M and whose diazomethane concentration was 1.5×10^{-1} M gave a 26.5% yield of II, 13.1% of triphenylmethane, 20.7% of triphenylethylene, and 8.1% of 1,1,2-triphenylethane. When the initial concentration of hexaphenylethane was 2.7×10^{-3} M and the diazomethane concentration was 2.7×10^{-2} M the yields were 5.4, 25.3, 32.7, and 7.3%, respectively. The changes in product ratios with changes in concentrations are indicative of competing processes with different kinetic orders. These data are satisfactorily accommodated if a 2,2,2-triphenylethyl radical is formed during the reaction sequence and it undergoes intramolecular rearrangement which is in competition with combination with triphenylmethyl to give II. The route by which

$$(C_6H_5)_3CCH_2\cdot + (C_6H_5)_3C\cdot \longrightarrow \text{II}$$
$$(C_6H_5)_2\overset{\cdot}{C}CH_2C_6H_5 \longrightarrow \text{products}$$

the 2,2,2-triphenylethyl radical is formed is not defined in detail by these studies; however, an addition to diazomethane followed by loss of nitrogen seems most likely. The intermediate azo radical probably loses

$$(C_6H_5)_3C\cdot + CH_2{=}\overset{+}{N}{=}\overset{-}{N} \longrightarrow (C_6H_5)_3CCH_2N{=}N\cdot$$
$$\text{III}$$
$$(C_6H_5)_3C\cdot$$
$$(C_6H_5)_3CCH_2N{=}NC(C_6H_5)_3 \quad (C_6H_5)_3CCH_2\cdot + N_2$$
$$\text{IV}$$
$$[(C_6H_5)_3CCH_2\cdot \quad N_2 \quad \cdot C(C_6H_5)_3] \longrightarrow \text{products}$$

nitrogen rapidly to give the 2,2,2-triphenylethyl radical which then reacts by rearrangement or reaction with triphenylmethyl. Reaction of III with triphenylmethyl to give the azo compound IV cannot be completely excluded. It cannot be the only mode of reaction for III because then decomposition of IV should yield essentially the same amounts of unrearranged *vs.* rearranged materials irrespective of the concentrations of reactants. Loss of nitrogen from III is probably ex-

and it also has steric interactions like those of the hexasubstituted ethanes. These two factors then should make this material less stable than either of the two kinds of ethanes and thus one predicts with a high degree of certainty that 1,1,1,2,2,3-hexaphenylpropane will be very unstable indeed. In fact the substance, II, showed no change in melting point after standing at 25° in the presence of air for 15 months.

(9) Rearrangement of the 2,2,2-triphenylethyl cation and carbanion are known and thus these intermediates cannot be absolutely excluded from consideration. There is, however, no obvious way in which they can be formed by reaction of triphenylmethyl with diazomethane and so they will not be given further consideration.

ceedingly fast[10] and there seems to be very little reason for considering that IV can be formed in any appreciable quantity.

Unfortunately, the results of these experiments do not permit an accurate assessment of the rate of rearrangement of the 2,2,2-triphenylethyl radical; however, it must be a relatively fast process to be able to compete with hexaphenylpropane formation.

Experimental Section[11]

Triphenylmethyl. Trityl chloride, 22.0 g, in 200 ml of dry benzene was stirred under nitrogen for 20 hr with 77.0 g of mercury. The resulting solution was filtered by forcing it under nitrogen pressure through a filter stick. The yield of triphenylmethyl was determined by allowing an aliquot of the solution to react with oxygen. Insoluble trityl peroxide is formed under these conditions. Yields of triphenylmethyl were 70–77%.

Reaction of Triphenylmethyl with Diazomethane in Benzene. Solutions of diazomethane in benzene were prepared by decomposing p-toluenesulfonylnitrosamide and entraining the liberated diazomethane in a stream of nitrogen. The diazomethane–nitrogen gas mixture was then allowed to bubble through cold benzene.

A solution of 1.3 g (0.031 mole) of diazomethane in 90 ml of benzene was added to a stirred solution of 7.1 g (0.029 mole) of triphenylmethyl in 250 ml of benzene. The resulting solution was stirred under nitrogen at 25° for 75 min. At that time a solution of 1.5 g (0.036 mole) of diazomethane in 100 ml of benzene was added. The orange-red color of the triphenylmethyl disappeared ca. 135 min after the initial addition of the diazomethane. The reaction mixture was allowed to stand under nitrogen at 25° for 24 hr.

In another experiment 7.5 g (0.031 mole) of triphenylmethyl in 250 ml of benzene was added dropwise over a period of 3 hr to a stirred solution of 1.3 g (0.031 mole) of diazomethane in 2.2 l. of benzene. After 75 min a solution of 1.5 g (0.036 mole) of diazomethane in 100 ml of benzene was added. The reaction mixture was allowed to stand under nitrogen for 20 hr.

Product Isolation. The benzene solutions were evaporated to 30 ml and then treated with 20 ml of hexane. The resulting solutions were cooled for 2 hr in an ice bath. The mixtures were filtered to remove trityl peroxide, and then the solvents were removed *in vacuo* to give a dark oil which was treated with 40 ml of a solution of methanol–acetone, 3:1. A white crystalline material precipitated, mp 200–214°. A small amount of the same material was obtained as a residue after evaporatively distilling the oil obtained after removing the methanol and acetone. The melting points

were raised to 218.5–219.8° (lit.[2,3] 216°) after recrystallization from acetic acid. The yields were 1.91 (26.5%) and 0.42 g (5.4%). The nmr spectra were identical with that reported.[2] The molecular weight was found to be 496 (calcd for $C_{39}H_{32}$: 500), by the Rast method.

The oily distillate obtained above had a singlet at 5.45 ppm which is characteristic of the methine proton in triphenylmethane. Gas–liquid chromatography of the distillate on a silicone gum column at 180° showed that there was a material present whose retention time was identical with that of triphenylmethane. Triphenylmethane was isolated from a preliminary experiment by chromatographing the reaction mixture, after removal of excess solvent, on silica gel. Elution with benzene–hexane, 1:3, afforded triphenylmethane, mp 88–91°, with no depression on admixture with an authentic sample. The yields of triphenylmethane were obtained by glpc using dicumyl as an internal standard.

The molecular distillate had a maximum absorption in the ultraviolet at 300 mμ; reported for triphenylethylene 300 mμ.[5] Glpc analysis on a silicone gum column at 180° showed a material with a retention time identical with that of triphenylethylene. The yields of triphenylethylene were calculated from ultraviolet and glpc data. Good agreement was obtained between the two methods.

The nmr spectrum of the molecular distillate had a doublet at 3.2 ppm ($J = 8$ cps) and a triplet at 4.1 ppm ($J = 8$ cps). These absorptions were also found in an authentic sample of 1,1,2-triphenylethane. Glpc analysis on a silicone gum column at 180° showed that a material was present whose retention time was identical with that of 1,1,2-triphenylethane. The yields of this substance were calculated from glpc data using dicumyl as an internal standard.

Reaction of Triphenylmethyl with Diazomethane in Ether. Reactions entirely similar to those reported above were conducted in ether solution. In one experiment the initial concentrations of triphenylmethyl and diazomethane were 8.7×10^{-2} M and 1.7×10^{-1} M, respectively. In this case the yields of products were: 1,1,1,3,3,3-hexaphenylpropane, 29.4%, triphenylmethane, 11.1%, triphenylethylene, 14.5%, and triphenylethane, 4.5%. In another experiment the initial concentration of triphenylmethyl was 1.6×10^{-3} M and the diazomethane was 3.2×10^{-2} M. The yields of products were: 1,1,1,3,3,3-hexaphenylpropane, 7.4%, triphenylmethane, 15.6%, triphenylethylene, 24.2%, and 1,1,2-triphenylethane, 8.9%. The nmr spectra of the crude reaction mixtures, containing broad aliphatic proton resonances at 0.9 and 1.2 ppm, indicated that some reaction with the solvent had occurred; however, no identifiable products could be isolated.

Thermal Decomposition of 1,1,1,3,3,3-Hexaphenylpropane. A sample, 0.103 g, of the material believed to be 1,1,1,3,3,3-hexaphenylpropane was heated at 250° for 1 hr in a sealed glass ampoule. The cooled product, a colorless oil, weighed 0.103 g. Glpc analysis showed that only two materials, whose retention times were identical with those of triphenylmethane and triphenylethylene, were present. The nmr spectrum had, besides absorptions in the aromatic region, an absorption at 5.45 ppm identical with that of triphenylmethane. The ultraviolet spectrum showed a maximum at 300 mμ which confirmed the presence of triphenylethylene.

(10) W. A. Pryor, "Free Radicals," McGraw-Hill Book Co., Inc., New York, N. Y., 1966, Chapter 10.

(11) Infrared spectra were recorded on a Perkin-Elmer Model 21 spectrometer. The ultraviolet spectra were obtained with a Cary Model 14 spectrometer. The nmr spectra were measured with a Varian Associates Model A-60 spectrometer; absorptions are reported in parts per million relative to tetramethylsilane as an internal standard.

Insertion Reactions of Nortricyclene with Ethyl Diazoacetate

R. R. Sauers and R. J. Kiesel

*Contribution from the School of Chemistry, Rutgers, The State University,
New Brunswick, New Jersey 08903. Received April 18, 1967*

Abstract: Photolysis of ethyl diazoacetate in the presence of nortricyclene (**2**) led to a mixture of esters **3** and **4**. The diminished reactivity of the bridgehead CH bond supports a charge-separated mechanism. No insertion on the C–C bond of the three-membered ring was observed.

One of the more intriguing reaction types in organic chemistry is the insertion reaction of carbenes (*e.g.*, eq 1). The experiments of Doering and Knox[1]

$$ \text{—CH} + :CH_2 \rightarrow \text{—CCH}_3 \qquad (1) $$
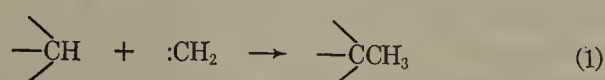
have yielded valuable information about the nature of the transition state of this "no-mechanism" reaction. In particular, it appears that charge separation is a useful hypothesis in the rationalization of the selectivity of various substituted carbenes toward primary, secondary, and tertiary carbon–hydrogen bonds.

Resonance forms of the type symbolized by **1** are expedient not only in providing a simple explanation of the relative reactivity of CH bonds, *i.e.*, primary <

$$ -\overset{|}{\underset{|}{C}}\text{---}H \longleftrightarrow -\overset{|}{\underset{|}{C}}+ \quad \overset{H}{\underset{R\diagup\diagdown R}{C}} $$

1
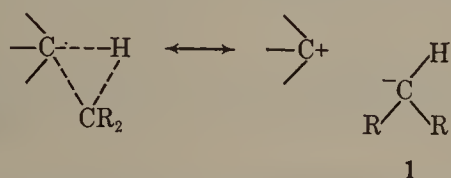
secondary < tertiary, but also in rationalizing the selectivity sequence: $(CH_3O_2C)_2C: > CH_3O_2CCH: \cdot \gg :CH_2$.[1]

It was of interest to examine the validity of these generalizations in other systems in which predictions concerning the ease of charge separation could be made. Specifically, the relative reactivity of a proton affixed to a bridgehead was to be evaluated. Diminution of the normal tertiary reactivity would lend support to a polarized transition state owing to the known difficulty in developing positive charge at bridgehead positions.[2]

For several reasons, it was decided to examine the reaction of ethyl diazoacetate with nortricyclene (**2**). Ethyl diazoacetate was chosen as the carbene precursor owing to the anticipated ease of product identification, although the selectivity would be modest at best (tertiary/secondary $\equiv$ 1.3[1]). Owing to symmetry, nortri-


2
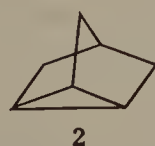
cyclene as a substrate is appealing since it has but three nonequivalent CH bonds. Additionally, the possibility of carbene insertion into the strained carbon–

carbon bond of the three-membered ring[3] was not an unreasonable alternative reaction pathway of interest.

Results and Discussion

A complex mixture of products was obtained upon irradiation of ethyl diazoacetate in nortricyclene. Owing to the relatively minor amounts of some of the constituents, it was decided to synthesize the products of major interest for the purposes of identification. Accordingly, we undertook preparation of esters **3**, **4**, and **5**.
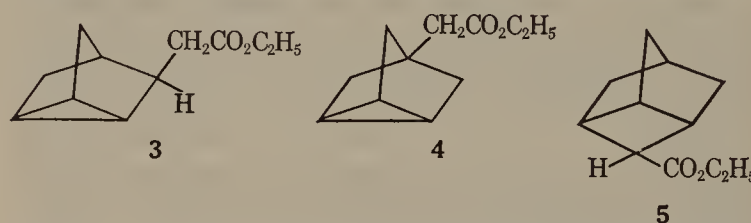
Ester **3** was readily available by homologation of 3-nortricyclenecarboxylic acid (**6**) *via* the Arndt–Eistert sequence.
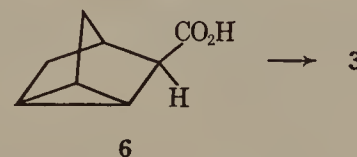
The availability of ester **4** depended on development of synthetic entries into the hitherto unknown 4-substituted nortricyclene system. 4-Chloronortricyclene (**8**) proved to be accessible *via* decomposition of the lithium salt of the *p*-tosylhydrazone[4] of 4-chloronorcamphor[5] (**7**). The appearance of typical nortricyclene
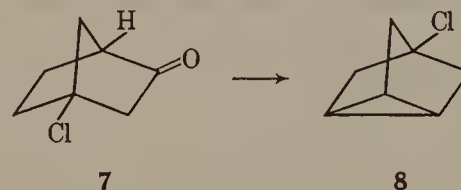
absorptions in the infrared spectrum at 12.5 μ[6] and the presence of two singlets of relative area 2:1 at 1.6 and 1.2 ppm[7] substantiated the structure of **8**. Metalation

(3) One such insertion into a C–C bond has been reported by K. B. Wiberg, G. M. Lampman, R. P. Ciula, D. S. Connor, P. Schertler, and J. Lavanish [*Tetrahedron*, **21**, 2729 (1965)]. A 1% yield of bicyclo-[1.1.1]pentane was reportedly formed from photolysis of diazomethane in bicyclo[1.1.0]butane.

(4) G. M. Kaufman, J. A. Smith, G. G. Vander Stouw, and H. Shechter, *J. Am. Chem. Soc.*, **87**, 935 (1965).

(5) K. B. Wiberg, B. R. Lowry, and T. H. Colby, *ibid.*, **83**, 3998 (1961).

(6) J. D. Roberts, E. R. Trumbull, Jr., W. Bennett, and R. Armstrong, *ibid.*, **72**, 3116 (1950).

(7) Nortricyclene shows three singlets at 1.2, 1.0, and 1.9 ppm in the area ratios of 6:3:1.

(1) W. von E. Doering and L. H. Knox. *J. Am. Chem. Soc.*, **83**, 1989 (1961).

(2) R. C. Fort and P. von R. Schleyer, "Advances in Alicyclic Chemistry," Vol. I, H. Hart and G. Karabatsos, Ed., Academic Press Inc., New York, N. Y., 1966, Chapter 5.

of **8** with lithium dispersion, followed by carboxylation and homologation, yielded ethyl 4-nortricyclylacetate (**4**) without complication.

Initial efforts to prepare 4-substituted derivatives of tricyclo[3.2.1.0³,⁶]octane were patterned after the original synthesis of this system.[8] Treatment of the epoxy ester **9** with sodium hydride failed to yield significant amounts of material with the expected volatility. In a closely related sequence, the esters **10** underwent cyclization on treatment with potassium *t*-butoxide. Small

9

10
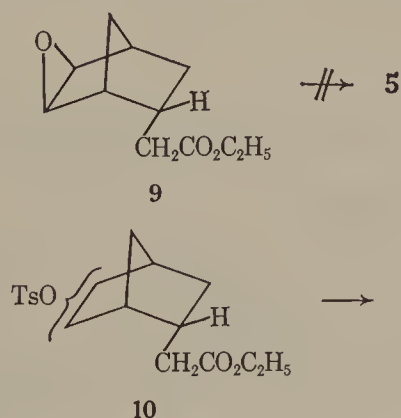
amounts of olefinic products were removed by potassium permanganate treatment, and the residue consisted of a 3:1 mixture of tricyclic esters with the required elemental composition. Degradation of **5** to the known hydrocarbon[8] tricyclo[3.2.1.0³,⁶]octane (**13**) *via* the Hunsdieker reaction and reduction of the bromide **12** (eq 2) established the structure of **5** beyond doubt. None of the isomeric hydrocarbon, tricyclo[3.3.0.0³,⁷]-octane, was detected.[9]
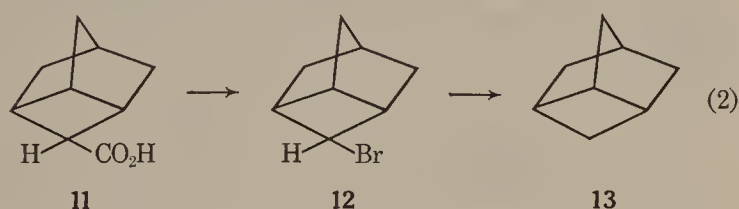
The relative amounts of esters **3** and **4** produced in the insertion reaction could now be evaluated. The observed ratio was found to be 14.8:1. The significance of this ratio can be best appreciated by a comparison with the "expected" ratio, calculated assuming normal reactivity of both types of hydrogens. This treatment yields a value of 4.6:1 for the predicted ratio of **3**:**4** taking into account both the statistical and the selectivity factors. These data suggest that either the methylene carbon–hydrogen bonds are unusually reactive or the bridgehead bond is unusually unreactive. A decision in favor of the latter alternative was made on the basis of the results of a competition experiment carried out with a mixture of nortricyclene and cyclohexane.

It was found that, in fact, the methylene groups of nortricyclene were less reactive than the methylene groups of cyclohexane by a factor of 0.67.

Clearly, the bridgehead C–H bond is unusually unreactive in nortricyclene. Steric considerations would lead one to expect at least no more hindrance to approach at this center than the corresponding bond in isobutane. The angular distortions in this system

probably allow greater accessibility of this bond than in aliphatic counterparts.

An electronic rationale is favored, therefore, and the original arguments of Doering and Knox[1] seem well suited for this purpose.[10]

Although no insertion into the C–C bonds was observed, a third product was observed. It is presumed that this material has structure **14** (see Experimental Section). Insertion on the C–H bonds of the cyclo-

14
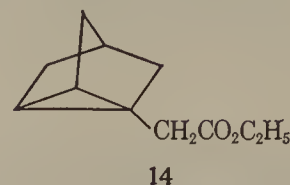
propyl ring would be expected to be even more unfavorable than insertion at the bridgehead owing to the well-known instability of cyclopropyl cations. Although there are three equivalent cyclopropyl C–H bonds, insertion at the bridgehead was evidently more favorable as seen from the ratio of **4**:**14** (*ca.* 1:2.8).

Experimental Section

Analyses are by Micro-Tech Labs, Skokie, Ill. Infrared spectra were determined on a Perkin-Elmer Model 21 or a Beckman Model 5A spectrometer in carbon tetrachloride or as noted. Nuclear magnetic resonance spectra were obtained from a Varian Model A-60 spectrometer in carbon tetrachloride unless otherwise noted. Chemical shifts are expressed in parts per million downfield from internal tetramethylsilane. Gas chromatograms were determined on an Aerograph Model A 90-P instrument and a Barber-Colman Model 5000 instrument in the case of capillary chromatograms. Melting points were determined on a Mel-Temp apparatus and are uncorrected.

Reaction of Ethyl Diazoacetate with Nortricyclene (2). A solution of 0.057 g (0.5 mmole) of ethyl diazoacetate and 0.807 g (8.6 mmoles) of nortricyclene in two drops of pentane was irradiated with a sunlamp, type RS (275 w), for 4 hr. Nitrogen evolution had essentially ceased at this point. Analysis of the resulting mixture by gas chromatography (150 ft × 0.01 in. Apiezon L, 130°) revealed three major products in the ratios 15.0:5.3:78.6 (**14**:**4**:**3**). The same values ±0.5% were obtained in a second experiment.

Preparative gas chromatography on a 15-ft Carbowax column at 160° yielded sufficient amounts of **3**, **4**, and **14** for spectral purposes. The nmr and infrared spectrum of **3** matched those of the sample prepared below. The nmr spectrum of **4** coincided with that obtained for this compound from the route described below. The infrared spectrum of the compound assigned structure **14** showed a carbonyl absorption at 5.82 μ and a strong band at 9.72 μ. The nmr spectrum showed the ethyl quartet at 4.1 ppm and a singlet at 2.4 ppm which was assigned to the methylene group adjacent to the carbonyl function. Complex absorption extended from 2.2 to 1.0 ppm.

Reaction of Ethyl Diazoacetate with Cyclohexane and Nortricyclene. A mixture of 5.0 g (0.053 mole) of nortricyclene, 2.2 g (0.0265 mole) of cyclohexane, and 1.7 g (0.0158 mole) of ethyl diazoacetate was irradiated with the sunlamp for 18 hr. A stream of running water flowing over the reaction flask was used for cooling. Most of the cyclohexane was removed by distillation, and the resulting mixture was analyzed by gas chromatography. The area ratio of the ethyl cyclohexylacetate:ethyl 3-nortricyclylacetate peak was 2.4:1. The molar ratio was calculated to be 60:40, respectively, based on comparisons with relative areas of a weighed mixture of the two. The identity of ethyl cyclohexylacetate was established by comparison of nmr and infrared spectra of a collected sample with those of an authentic sample.[1]

4-Chloronorcamphor Tosylhydrazone. A solution of 37.2 g (0.20 mole) of tosylhydrazine in 100 ml of hot glacial acetic acid was added in portions to a solution of 60 g (0.41 mole) of crude 4-

(8) R. R. Sauers and R. A. Parent, *J. Org. Chem.*, 28, 605 (1963); R. R. Sauers, R. A. Parent, and S. B. Damle, *J. Am. Chem. Soc.*, 88, 2257 (1966).

(9) P. K. Freeman, V. N. M. Rao, and G. E. Bigam, *Chem. Commun.*, 21, 511 (1965).

(10) Similar conclusions were reached by M. R. Willcott, III, Ph.D. Thesis, Yale University, 1963.

chloronorcamphor (7)[11] in 50 ml of glacial acetic acid. There was obtained a crystalline precipitate on standing overnight at room temperature. The product was removed by filtration and washed with water. Recrystallization from ethanol–water gave 40 g (70%) of 4-chloronorcamphor tosylhydrazone, mp 176–178°.

Anal. Calcd for $C_{14}H_{17}O_2SCl$: C, 53.75; H, 5.44; N, 8.93. Found: C, 53.73; H, 5.45; N, 8.90.

4-Chloronortricyclene (8). A solution of 35 ml of 1.6 N *n*-butyllithium in hexane (*ca.* 0.056 mole) was injected through a serum cap over 5 min into a stirred slurry of the tosylhydrazone (15.65 g, 0.055 mole) in 200 ml of dry tetrahydrofuran. A nitrogen atmosphere was maintained throughout, and the temperature was kept at 0–5° during the addition and for 0.5 hr afterward. Stirring at room temperature for 0.5 hr was followed by evaporation of the solvent on a rotary evaporator at 40° (0.5 mm). The salt was then pyrolyzed by gradually raising the temperature to 175–225° whereupon 4-chloronortricyclene distilled from the flask. The vapors were condensed in a Dry Ice trap and distilled to give 4.0 g (62%) of 4-chloronortricyclene, bp 142–144°, n^{25}D 1.4814.

Anal. Calcd for C_7H_9Cl: C, 65.37; H, 7.00; Cl, 27.62. Found: C, 65.10; H, 7.19; Cl, 27.47.

The nmr spectrum displayed two singlets of relative area 2:1 at 1.6 and 1.2 ppm, respectively. Selected infrared bands appeared at 3.29 (w), 8.03 (s), and 9.95 (s) μ.

4-Nortricyclenecarboxylic Acid. To a refluxing mixture of *ca.* 3.0 g (0.22 g-atom) of lithium dispersion[12] and 25 ml of dry cyclohexane was added 5.14 g (0.04 mole) of 4-chloronortricyclene in 15 ml of cyclohexane. The addition required 0.5 hr, and the resulting mixture was heated at reflux for an additional 5 hr. The cooled mixture was poured over crushed Dry Ice and allowed to stand for several hours. The mixture was then cautiously treated with water followed by dilute hydrochloric acid. The liberated acid was extracted into methylene chloride which was washed with water and dried. Evaporation of the extract yielded 4.5 g of crude acid which was purified by crystallization from methylene chloride–pentane. White needles, mp 156–158°, were obtained in 67% (3.7 g) yield.

Anal. Calcd for $C_8H_{10}O_2$: C, 69.56; H, 7.24. Found: C, 69.33; H, 7.35.

The infrared spectrum (Nujol) of this product showed carbonyl absorption at 5.90 μ and the typical broad absorption for the hydroxyl group centered at 3.0 μ. The nmr spectrum (CHCl₃) displayed singlets at 1.6 (6 H), 1.2 (3 H), and 11.3 (1 H) ppm.

Ethyl 4-Nortricyclylacetate (4). A mixture of 3.2 g (0.023 mole) of the acid was heated at reflux for 3 hr with 20 ml of thionyl chloride. The excess thionyl chloride was removed *in vacuo*, and the residue was distilled to give 2.6 g (72%) of 4-nortricyclenecarbonyl chloride, bp 47° (4 mm).

To a cold solution containing approximately 6 g of diazomethane and 1.6 g of triethylamine in 500 ml of dry ether was added 2.5 g (0.016 mole) of the acid chloride over a period of 15 min. The resulting mixture was stirred for 2 hr at 0° and overnight at room temperature. Excess diazomethane was removed by passing a stream of nitrogen through the solution. The amine hydrochloride was removed by filtration, and the ether was evaporated to yield a yellow oil.

The crude diazo ketone in 10 ml of ethanol was added dropwise to a refluxing mixture of 1.5 g of silver oxide in 20 ml of ethanol. A second 1.5-g portion of silver oxide was added portionwise during the addition of the diazo ketone. The additions required 0.5 hr and reflux was continued for a 2-hr period beyond. The cooled solution was filtered and diluted with 200 ml of water. The product was extracted into pentane which was washed with sodium bicarbonate solution and water and dried over magnesium sulfate. The pentane was evaporated, and the residue was distilled to give 1.78 g (62%) of ester 4, bp 64–66° (1.5 mm).

Anal. Calcd for $C_{11}H_{16}O_2$: C, 73.24; H, 8.94. Found: C, 73.43; H, 9.07.

The infrared spectrum showed bands at 3.30 (m) and 5.78 (s) μ. The nmr spectrum displayed a quartet (2 H) at 4.0, a singlet (2 H) at 2.4, and two singlets at 1.3 and 1.1s uperimposed on a triplet at *ca.* 1.2 ppm (12 H).

Ethyl 3-Nortricyclylacetate (3). 3-Nortricyclenecarbonyl chloride, bp 49–50° (4 mm), was prepared in 83% yield by heating 3-nortricyclenecarboxylic acid (7.0 g) with 25 ml of thionyl chloride for 3 hr followed by distillation. The acid chloride (3.9 g) was

converted to the diazo ketone by the procedure mentioned. Treatment with silver oxide gave 2.7 g (60%) of the desired ester 3, bp 80–81° (2.5 mm).

Anal. Calcd for $C_{11}H_{16}O_2$: C, 73.24; H, 8.94. Found: C, 73.41; H, 9.11.

The infrared spectrum showed bands at 3.23 (m), 5.75 (s), 9.72 (s), and 12.52 (s) μ. The nmr spectrum showed a quartet (2 H) at 4.1 and complex absorption (14 H) between 2.2 and 0.9 ppm.

Ethyl Tricyclo[3.2.1.0³,⁶]octane-4-carboxylate. A mixture of 5-norbornene-2-acetic acids was converted to ethyl esters,[13] bp 68–70° (0.25 mm), *via* the acid chlorides. Hydroboration of the mixture was effected by addition of 15 ml of 1 *M* BH₃ in tetrahydrofuran to a solution of 7.2 g (0.04 mole) of esters in 10 ml of tetrahydrofuran at 0–5°. The addition time was 1 hr. After stirring for 2 hr at 0° and 1 hr at 25°, the mixture was treated with 5 ml of 30% hydrogen peroxide and 13 ml of 1 *M* sodium hydroxide solution at 5–15°. After an additional 2-hr stirring at 5°, excess water was added, and the mixture was extracted with ether. The dried extracts were distilled to give 5.6 g (71%) of mixed hydroxy esters, bp 107–108° (0.2 mm). The infrared spectrum of the mixture showed hydroxyl and carbonyl absorption at 2.97 and 5.84 μ, respectively.

The mixture of alcohols was converted to *p*-toluenesulfonate esters by treatment with tosyl chloride in pyridine. From 11.88 g of alcohols there was obtained 20.3 g of crude tosylates.[10]

Cyclization was effected by treatment of 5.7 g (0.016 mole) of tosylates with 1.79 g (0.016 mole) of potassium *t*-butoxide in 200 ml of benzene at 25°. The mixture was stirred overnight after which the benzene was washed with water and dried over magnesium sulfate. Evaporation of the benzene gave 1.4 g of an oil, bp 75–120° (0.25 mm). From two other runs there was obtained 12 g of this material. This fraction was washed with hot potassium permanganate solution to remove unsaturates. Distillation gave 3.0 g (12%) of the tricyclic esters, bp 82–85° (0.2 mm). A second fraction boiling from 85 to 110° (0.2 mm) was essentially pure ester.

Anal. Calcd for $C_{11}H_{16}O_2$: C, 73.24; H, 8.94. Found: C, 73.17; H, 8.97.

The infrared spectrum showed a carbonyl stretching band at 5.85 μ. The nmr spectrum displayed a quartet at 4.1, broad multiplets at 3.1 and 2.5, a sharp singlet at 2.2, and complex absorptions between 1.7 and 1.1 ppm. Capillary gas chromatography (150 ft × 0.01 in. Apiezon L, 140°) indicated two components in an area ratio of *ca.* 3:1.

4-Tricyclo[3.2.1.0³,⁶]octanecarboxylic Acid (11). Hydrolysis of the ester (2.8 g) was effected by treatment with 1.7 g of potassium hydroxide in 50% aqueous ethanol for 7 hr at reflux. Evaporation of most of the ethanol was followed by acidification and ether extraction to yield 2.2 g (93%) of crude acid. After crystallization from pentane and sublimation the acid had mp 76–78°.

Anal. Calcd for $C_9H_{12}O_2$: C, 71.05; H, 7.89. Found: C, 71.16; H, 7.99.

The nmr spectrum (CHCl₃) showed a singlet at 11.9 (1 H), a crude triplet at 3.1 (1 H), broad singlet at 2.5 (3 H), sharp singlet at 2.3 (1 H), and broad singlets at 1.6 (4 H) and 1.3 (2 H) ppm.

4-Bromotricyclo[3.2.1.0³,⁶]octane (12). The silver salt of the acid 11 was prepared by treatment of 2.0 g (0.013 mole) of acid in 20 ml of water with sufficient ammonium hydroxide to effect salt formation. The excess ammonia was removed by gentle heating, and the silver salt was precipitated by addition of a solution of 2.2 g (0.013 mole) of silver nitrate in 30 ml of water. The salt was collected on a filter and washed with water, ether, and alcohol. After drying overnight at 115°, the weight of salt was 3.0 g. This product was suspended in 50 ml of dry petroleum ether (bp 30–60°) and cooled to −10°. Bromine (2.0 g, 0.012 mole) in 10 ml of petroleum ether was added dropwise with stirring, and the resulting mixture was stirred at −10° for 1 hr. After an additional hour at 25° and one at reflux the mixture was filtered to remove the salts. Distillation gave 0.72 g (29%) of the bromide, bp 52° (2.2 mm).

Anal. Calcd for $C_8H_{11}Br$: C, 51.38; H, 5.88; Br, 42.73. Found: C, 51.52; H, 6.16; Br, 42.38.

Strong infrared absorptions appeared at 8.12, 8.48, 9.93, 11.0, 13.0, and 14.4 μ. The nmr spectrum showed a sharp singlet at 3.8, a broad singlet at 3.4, and complex absorption extending from 3.0 to 1.0 ppm. Based on the total integrated area, the two low-field peaks accounted each *ca.* 0.8 proton. It is not unlikely that a mixture of bromides was present.

Tricyclo[3.2.1.0³,⁶]octane (13). To a stirred suspension of 0.50 g of sodium in 15 ml of liquid ammonia was added 0.60 g of bromide 12. The mixture was allowed to warm to room temperature at

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(11) Prepared from 1-chloronorbornane by the method of J. Bredt and P. Pinten, *J. Prakt. Chem.*, **115**, 45 (1927). From 60 g of 1-chloronorbornane was obtained 60 g of crude 7.

(12) Available as a 50% slurry in hexane.

(13) K. Alder and E. Windemuth, *Ber.*, **71**, 1939 (1938).

which time 75 ml of pentane was added followed by dropwise addition of water. The pentane layer was separated and dried over magnesium sulfate. The pentane was evaporated to yield an oil. Essentially one peak was present on a gas chromatogram on a 15-ft Carbowax column at 90°. A 60-mg sample was collected and submitted to nmr analysis. The spectrum was identical with that of a sample prepared earlier.[8]

On the Chemistry of Reactions Proceeding inside Molecular Aggregates

F. M. Menger and Carolyn E. Portnoy

Contribution from the Department of Chemistry, Emory University, Atlanta, Georgia 30322. Received April 7, 1967

Abstract: The rate constants for basic hydrolysis of *p*-nitrophenyl acetate, mono-*p*-nitrophenyl dodecanedioate, *p*-nitrophenyl octanoate, and benzoylcholine chloride (two neutral and two ionic substrates) were determined in surfactant solutions containing varying amounts of either laurate anion, *n*-dodecyltrimethylammonium cation, or *n*-dodecylpyridinium cation. Laurate inhibits hydrolysis of all four esters, *n*-dodecyltrimethylammonium cation enhances the rates, and *n*-dodecylpyridinium cation has very little effect. A kinetic scheme is proposed for the laurate system which involves partitioning of the substrates between the solution and the micellar phases. It is possible to evaluate both the substrate–micelle association constants (which are very large numbers and exceed those for many enzyme-specific substrate complexes) and the rate constants for adsorbed ester (which are within experimental error of zero). The kinetic data are discussed in terms of the complex structure of micelles.

The living cell contains a large number of particles composed of aggregates of molecules.[1] The particles associate to form subcellular bodies such as mitochondria and chloroplasts. Thus, life processes proceed mainly within complicated assemblages of molecules rather than in the free solution (where control of the reactions would be difficult). A knowledge of chemical behavior inside molecular aggregates is essential to the understanding of these highly organized biological processes. Consequently we have begun a study of the subject and present our initial results in this paper. The report concerns reactions occurring inside one particular type of biologically important aggregate,[2] the micelle. Micelles are formed in aqueous solutions by surfactants, which are compounds possessing a water-solubilizing moiety (often an ionic group) and a water-insoluble portion (a long hydrocarbon chain). Micelles are spherical aggregates, of 30 or more molecules, containing hydrocarbon interiors and ionic surfaces.[3]

Several examples have appeared recently of organic reactions whose rates are perturbed by the presence of small quantities of surfactant. The acid hydrolysis of benzylideneaniline to benzaldehyde and aniline is inhibited by cetyltrimethylammonium bromide.[4] Duynstee and Grunwald[5] showed that surfactants affect the rate of dye fading, and Kurz[6] found that acid-catalyzed hydrolysis of long-chain sodium alkyl sulfates is accelerated, and base-catalyzed hydrolysis inhibited, by micellation. Other reactions that have been studied in the presence of surfactants include the hydrolysis of Schiff bases[7] and esters,[8] the reaction of 1-fluoro-2,4-dinitrobenzene with amines,[9] and porphyrin–metal interaction.[10] Letsinger and Wagner[11] used cationic and anionic surfactants to regulate the rate of reaction of a polyuridylic acid derivative.

In this paper we elucidate the dependence of the rate constants for basic hydrolysis of four substrates A–D on the concentration of each of the three surfactants E–G. We selected ester hydrolysis for study

Substrates	Surfactants
$CH_3COOC_6H_4NO_2$	$^-OOC(CH_2)_{10}CH_3$
A	E
$^-OOC(CH_2)_{10}COOC_6H_4NO_2$	$(CH_3)_3N^+(CH_2)_{11}CH_3$
B	F
$CH_3(CH_2)_6COOC_6H_4NO_2$	$C_5H_5N^+(CH_2)_{11}CH_3$
C	G
$(CH_3)_3N^+CH_2CH_2OOCC_6H_5$	
D	

because it can be followed spectrophotometrically at very low substrate concentrations where the structure of the micelles, formed by the surfactants, is not

(1) J. L. Fairley and G. L. Kilgour, "Essentials of Biological Chemistry," Reinhold Publishing Corp., New York, N. Y., 1966, p 120.

(2) P. K. Brown, I. R. Gibbons, and G. Wald, *J. Cell Biol.*, **19**, 79 (1963).

(3) (a) D. J. Shaw, "Introduction to Colloid and Surface Chemistry," Butterworth & Co. (Publishers) Ltd., London, 1966; (b) L. I. Osipow, "Surface Chemistry," Reinhold Publishing Corp., New York, N. Y., 1962.

(4) K. G. van Senden and C. Koningsberger, *Tetrahedron*, **22**, 1301 (1966).

(5) E. F. J. Duynstee and E. Grunwald, *J. Am. Chem. Soc.*, **81**, 4540 (1959).

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(7) M. T. A. Behme and E. H. Cordes, *J. Am. Chem. Soc.*, **87**, 260 (1965).

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(9) D. G. Herries, W. Bishop, and F. M. Richards, *J. Phys. Chem.*, **68**, 1842 (1964).

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(11) R. L. Letsinger and T. E. Wagner, *J. Am. Chem. Soc.*, **88**, 2062 (1966).

perturbed. Moreover, basic hydrolysis of esters is a thoroughly understood reaction and one that is free from complications. Two of the substrates are neutral and two are ionic. Neutral ester C possesses a long hydrocarbon chain and is extremely water insoluble. Anionic substrate B is itself a surfactant; its labile ester moiety is distant from the ionic site. Thus, if molecule B is positioned in the micelle as are the surfactant molecules making up the micelle, then the ester group of B will be buried well within the hydrocarbon interior of the aggregate. On the other hand, the cationic benzoylcholine (D) is a short molecule. If its charged portion is forced to reside on the surface of a micelle near the water, then the reactive ester group cannot penetrate very deeply into the micelle interior. The surfactants possess important structural differences as well. Laurate anion (E) forms micelles with highly charged negative surfaces. If ester groups of a substrate are adsorbed onto a micelle surface, then nucleophilic carboxylate catalysis is a possibility. The micelles of the two cationic surfactants F and G differ in the degree of exposure of the ionic atoms, and it was of interest to determine whether this difference would manifest itself kinetically.

In summary, the purpose of this work is to determine the effect of substrate and surfactant structure on kinetic parameters in order to understand better the nature of substrate–surfactant interaction and micellar reactions in general.

Experimental Section

Materials. *p*-Nitrophenyl Acetate (A). This compound was prepared by the method of Chattaway[12] and recrystallized repeatedly until it was nearly colorless; mp 77–78° (lit.[13] mp 77.5–78°).

Mono-*p*-nitrophenyl Dodecanedioate (B). Dodecanedioic acid (2.0 g, 8.7 × 10⁻³ mole) (Matheson Coleman and Bell, recrystallized from EtOAc) and 1.0 g (4.3 × 10⁻³ mole) of *p*-nitrophenyl trifluoroacetate (Aldrich) were dissolved in 15 ml of dry pyridine and allowed to react at room temperature for 30 min. The solution was poured into 60 ml of ice water, and the resulting yellow precipitate was collected by filtration. The dried solid was crystallized once from benzene–hexane and several times from MeOH; mp 85.5–87°. The diacid is appreciably more soluble in MeOH, and the diester appreciably less soluble, than the monoester. *Anal.* Calcd for $C_{18}H_{25}NO_6$: C, 61.52; H, 7.17; N, 3.99. Found: C, 61.39; H, 6.99; N, 4.08.

***p*-Nitrophenyl Octanoate (C).** Substrate C, an oil, was obtained from Pierce Chemical Co. and was used without further purification.

Benzoylcholine Chloride (D). The ester was obtained commercially (Pierce), recrystallized twice from EtOH–EtOAc (1:5), and dried at 100° under reduced pressure for 12 hr; mp 206–207° (lit.[14] mp 204–205°).

Lauric Acid (E). The Eastman product was crystallized from MeOH and dried thoroughly. Its identity was checked by a mixture melting point determination.

***n*-Dodecyltrimethylammonium Bromide (F).** We thank Glovers Ltd. for a generous supply of the material marketed as Morpan D. It was recrystallized from purified acetone and dried at 100° under reduced pressure for 1 hr; mp 241.5–243.5° (lit.[15] mp 243°).

***n*-Dodecylpyridinium Chloride (G).** We were unable to obtain satisfactory material by recrystallizing commercially available surfactant and therefore prepared it ourselves from pyridine and the alkyl chloride.[16] Beautiful white crystals were obtained after

many recrystallizations, but they melted at 68–72° (lit.[16] mp 86–87°). Drying them under high vacuum at 60° over P_2O_5 did not change the melting point. The melting behavior of the pyridinium salt was characteristic of a smectic mesophase and possibly the melting point disparity is related to this fact. Gravimetric analysis for chloride ion indicated that the *n*-dodecylpyridinium chloride (also called laurylpyridinium chloride) was pure.

All inorganic compounds were of reagent quality. Methanol was distilled once over magnesium.

Kinetics. The procedure is given here for one particular substrate and surfactant, and it is typical of that which was used throughout. Lauric acid (0.5402 g), NaOH (0.1 g), and KCl (1.603 g) were weighed out in a 50-ml volumetric flask. The flask was then filled to the mark with 0.02 *N* NaOH. The pH of the resulting solution (0.05 *M* laurate, *I* = 0.5) was adjusted to pH 12.14 ± 0.02 with the aid of a Corning Model 12 pH meter. The less concentrated laurate solutions were prepared from the 0.05 *M* laurate by diluting portions of it with aqueous base (pH 12.14, *I* = 0.5) containing no surfactant.

A cuvette was filled with 3.00 ml of one of the laurate solutions, stoppered, and placed in the thermostated chamber (25.0 ± 0.1°) of a Cary 14 PM recording spectrophotometer. After about 15 min, 25 μl of an aqueous solution of benzoylchloline chloride (prepared immediately before the spectrophotometry) was added to the cuvette with the aid of a small stirring rod flattened at one end. The decrease in absorbance at 274 mμ was then traced as a function of time. The hydrolysis of the ester (initial concentration: 8.65 × 10⁻⁴ *M*) was usually followed to completion. A final pH reading was taken to ensure that no pH change had occurred during the reaction.

The runs with the *p*-nitrophenyl esters were performed in sodium borate buffers of lower pH values at which the laurate was insoluble. Hence, it was necessary to carry out the kinetics at 50°. The pH measurements of the buffers were also made at 50° after standardizing the meter at this temperature using 0.01 *M* sodium borate (pH (at 50°) 9.01[17]). There is no such solubility problem with the cationic surfactants, and all the runs using these were performed at 25°. The hydrolyses of the *p*-nitrophenyl esters were studied in the same manner as described above except that the substrates were dissolved in methanol and an increase in absorbance at 400 mμ, due to *p*-nitrophenolate liberation, was utilized to follow the reactions.

First-order plots were linear to greater than 80% of the reactions. Duplicate runs agreed to better than 4%.

Critical Micelle Concentration. The concentration at which a surfactant abruptly associates into micelles is called its critical micelle concentration (CMC). The CMC of laurate at 50°, pH 9.59, was determined by the spectral-change technique[18] (which is not as accurate as other methods but which is very convenient particularly when the temperature must be elevated). Each of the laurate solutions used in the kinetic runs was equilibrated in a cuvette at 50° inside a Cary 14 compartment and the absorbance at 610 mμ was adjusted to zero. A methanolic solution of pinacyanol chloride (25 μl) was added to obtain a dye concentration of 1.05 × 10⁻⁵ *M*. An absorbance reading was then taken. A plot of absorbance *vs.* laurate concentration shows a striking change at 0.009 *M*. The CMC of laurate at the specified conditions is assigned this value. A spectrophotometer is in fact unnecessary for the CMC determination: above the CMC the solutions are a bright blue, while below it they are a light shade of pink.

Results

The rate constants for hydrolysis of *p*-nitrophenyl acetate (A), mono-*p*-nitrophenyl dodecanedioate (B), and *p*-nitrophenyl octanoate (C) at pH 9.59, 50°, in the presence of varying amounts of laurate (E) are plotted in Figure 1. The curves were constructed from rate data such as those given in Table I. The hydrolysis rates of the three esters in the absence of laurate differ from each other by only a small factor, indicating that neither B nor C is in any way an unusual substrate due to intramolecular carboxylate catalysis or to "burying" of the ester group in a folded hydrocarbon chain. The

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(17) R. G. Bates, *J. Res. Natl. Bur. Std.,* **66A,** 179 (1962).
(18) M. L. Corrin, H. B. Klevens, and W. D. Harkins, *J. Chem. Phys.,* **14,** 480 (1946).
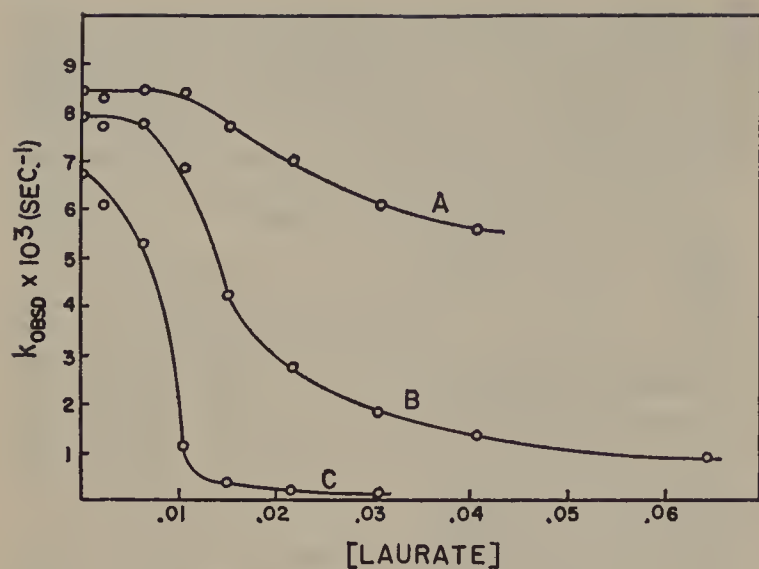
Figure 1. Plots of observed rate constants for the hydrolysis of p-nitrophenyl acetate (A), a mono-p-nitrophenyl dodecanedioate (B), and p-nitrophenyl octanoate (C) at pH 9.59, $I = 0.1$, 50.0°, vs. concentration of laurate. The rate constants of A have been divided by 2.00 to bring the curve on scale.
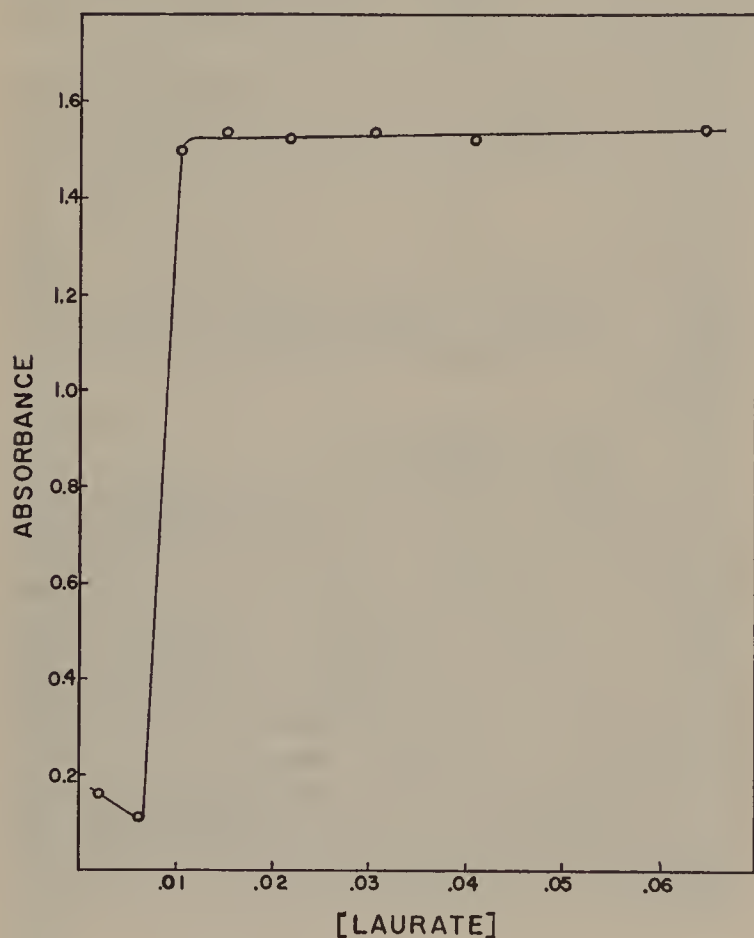

Figure 2. The absorbance of 1.05×10^{-5} M pinacyanol chloride at 610.0 mμ in pH 9.59 sodium borate buffer ($I = 0.1$) at 50.0° vs. laurate concentration.

plots show that laurate significantly inhibits hydrolysis of the esters, but that the effect is large only above 0.01 M laurate. This is the concentration (the critical micelle concentration) at which laurate abruptly associates into micelles, a fact demonstrated in Figure 2. In this graph the absorbance at 610 mμ of 1.05×10^{-5} M pinacyanol chloride (under conditions identical with those used for the kinetic runs) is plotted vs. [laurate]. The sudden increase in absorbance is caused by absorption of the dye onto or into the soap micelles.[18] The shapes of the curves of Figure 1 prove that simple
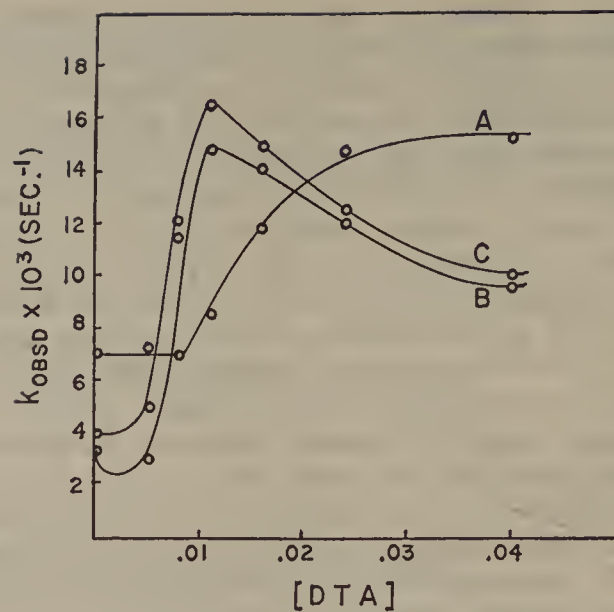

Figure 3. Plots of observed rate constants for the hydrolysis of p-nitrophenyl acetate (A), mono-p-nitrophenyl dodecanedioate (B), and p-nitrophenyl octanoate (C) at pH 10.49, $I = 0.2$, 25.0°, vs. concentration of n-dodecyltrimethylammonium bromide (DTA).

1:1 complexation between substrate and surfactant cannot be the cause of the rate inhibitions.[19] Clearly, interaction between the esters and *micellar* surfactant is the source of the rate perturbations.

Table I. The Observed Rate Constants for Hydrolysis of Mono-p-nitrophenyl Dodecanedioate in Laurate Solutions[a]

(Laurate) $\times 10^2$, M	$k_{obsd} \times 10^3$, sec^{-1}
0.00	7.90
0.216	7.69
0.634	7.78
1.05	6.89
1.52	4.22
2.17	2.78
3.06	1.84
4.08	1.40
6.48	0.94

[a] In 0.8% methanol–water (v/v) at 50.0°; pH 9.59; $I = 0.1$; ester concentration = 5.79×10^{-5} M.

The inhibitory effect of laurate is strongly dependent on the structure of the substrate. While 0.02 M laurate reduces the rate of hydrolysis of C to 4% of that in the absence of surfactant, the reactivity of A is lowered to only 83% of normal. In all the kinetic runs the initial substrate concentration was well below 10^{-4} M, making it very unlikely that the difference in behavior between the substrates is caused by one of them inducing micellation or else seriously perturbing the structure of the micelles. In this connection it is important to note that the reactions were first order in substrate at the high dilutions. The causes for the rate differences will be discussed in the following section.

In Figure 3 the dependence of the rate constants for hydrolysis of A, B, and C at pH 10.49, 25°, on the concentration of n-dodecyltrimethylammonium cation (F) is presented. The bell-shaped curves are similar to that found for basic hydrolysis of benzylideneacetophenone in cetyltrimethylammonium ion solutions.[4] n-Dodecylpyridinium ion (G), on the other hand, has hardly

(19) F. M. Menger and M. L. Bender, *J. Am. Chem. Soc.*, **88**, 131 (1966).
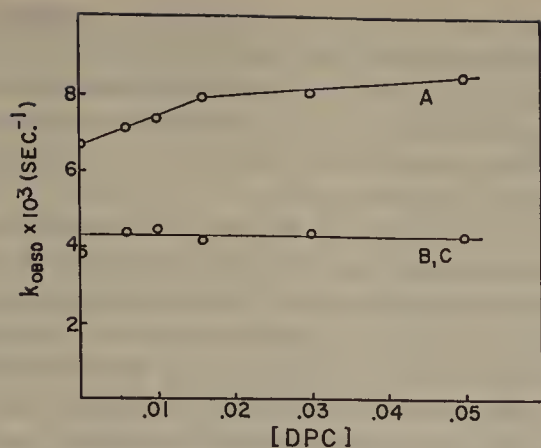
Figure 4. Plots of observed rate constants for the hydrolysis of p-nitrophenyl acetate (A), mono-p-nitrophenyl dodecanedioate (B), and p-nitrophenyl octanoate (C) at pH 10.48, $I = 0.5$, 25.0°, vs. concentration of n-dodecylpyridinium chloride (DPC). Points for B and C are virtually superimposable.

Figure 5. Plots of observed rate constants for hydrolysis o benzoylcholine at pH 12.14, $I = 0.5$, 25.0°, vs. concentration o laurate (A) and n-dodecyltrimethylammonium bromide (B).

any effect on the hydrolysis of the three p-nitrophenyl esters (Figure 4). The rate constants for hydrolysis of our only cationic substrate, benzoylcholine (D), in laurate and n-dodecyltrimethylammonium ion solutions are given in Figures 5A and 5B, respectively.

Discussion

In a homogeneous surfactant solution (above the critical micelle concentration) the reactive site of a substrate may exist in one or more of the following environments: the micelle interior, the micelle–water interface, and the bulk solvent. A few comments about these regions are necessary for the understanding of our interpretation of the kinetic data.

The nature of the micelle interior, formed by the lyophobic portion of the surfactant, is not fully understood. From high-resolution nmr experiments it appears that (a) the center of the micelle is similar to liquid hydrocarbon[20] and that (b) water can penetrate the micelle[21] so that part of the alkyl chain, perhaps the first five carbons from the ionic group,[22] is exposed to the solvent. (In addition it is believed that folding of the chains in the interior is not extensive because the diameter of the Hartley spherical micelle is roughly twice that of the fully extended surfactant molecule.[23]) An ester substrate adsorbed into the very inner part of a micelle would be inert to hydroxide ion catalyzed hydrolysis because the anionic nucleophile is certainly absent in the hydrocarbon. Unfortunately, it is less clear what the effect would be of adsorption of an ester into the outer aqueous portion of the interior. If the micelle is a very compact unit, then most of the interior water will be highly structured; all available evidence[19,24] indicates that basic hydrolysis would be markedly impeded in such a situation. However, it is more likely that the micelle is a loose aggregation[25] and that the water within the micelle resembles bulk water containing some organic solvent. In this case the kinetic perturbation of adsorption would not be ex-
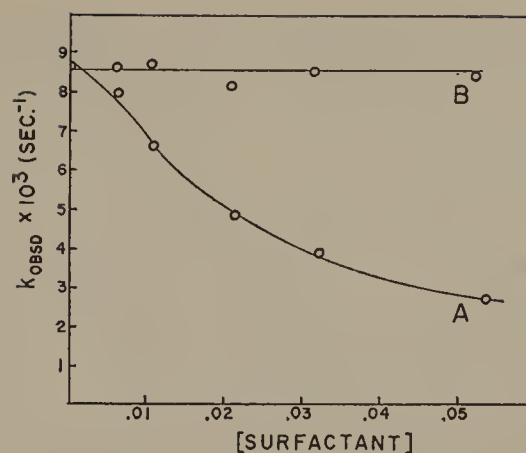
pected to be large. Long-range electrostatic effects originating from the charged micelle interface could well be the major factor affecting hydrolysis rates inside the interior aqueous shell.

The micelle surface is another possible site of substrate adsorption. The ionic portions of the surfactant molecules form highly charged surfaces which attract small counterions from the solution in order to relieve electrostatic repulsion. Thermal motion, which tends to produce uniform distribution of the ions, disturbs the ionic array resulting in the well-known diffuse electrical double layer. Basic ester hydrolysis is not very sensitive to ionic strength changes, so that the high concentration of ions at the double layer would not in itself greatly affect the reaction. However, adsorption of an ester at the surface of a cationic micelle could result in considerable rate enhancement because hydroxide ion (along with other anions) collect in this region. Several rate enhancements have been attributed to this phenomenon.[5,8]

A third possibility is that a substrate is not adsorbed by the micelles and exists in the free solution. The less water soluble a substrate, the more extensively it will be partitioned into the micellar phase.[26]

Little evidence exists at this time concerning where adsorption occurs within the micelle, but a particularly interesting article on this point has recently appeared. Eriksson and Gillberg[27] showed by resonance line shifts and line-width changes in the nmr that cetyltrimethylammonium bromide adsorbs cyclohexane and cumene into the inner hydrocarbon portion of the micelles, whereas N,N-dimethylaniline and nitrobenzene reside in the aqueous section of the interior not far from the surface.

We now direct attention to Figure 1 which shows that laurate micelles inhibit hydrolysis of p-nitrophenyl acetate (A), mono-p-nitrophenyl dodecanedioate (B), and p-nitrophenyl octanoate (C) with an increasing order of effectiveness.[28] The solubilities of the substrates in water decrease in the same order, suggesting that the differences in behavior between the substrates may be due, at least in part, to varying degrees of non-

(20) J. Clifford and B. A. Pethica, *Trans. Faraday Soc.*, **60**, 1483 (1964).
(21) J. Clifford, *ibid.*, **61**, 1276 (1965).
(22) M. J. Vold and R. D. Vold, "Colloid Chemistry," Reinhold Publishing Corp., New York, N. Y., 1964, p 63.
(23) H. B. Klevens, *Chem. Rev.*, **47**, 1 (1950).
(24) E. F. J. Duynstee and E. Grunwald, *Tetrahedron*, **21**, 2401 (1965).
(25) Reference 3b, Chapter 9.

(26) M. E. L. McBain and E. Hutchinson, "Solubilization and Related Phenomena," Academic Press Inc., New York, N. Y., 1955.
(27) J. C. Eriksson and G. Gillberg, *Acta Chem. Scand.*, **20**, 2019 (1966).
(28) The fact that surfactants have a larger effect on the hydrolysis of long-chain, as opposed to short-chain, esters has already been established.[8]
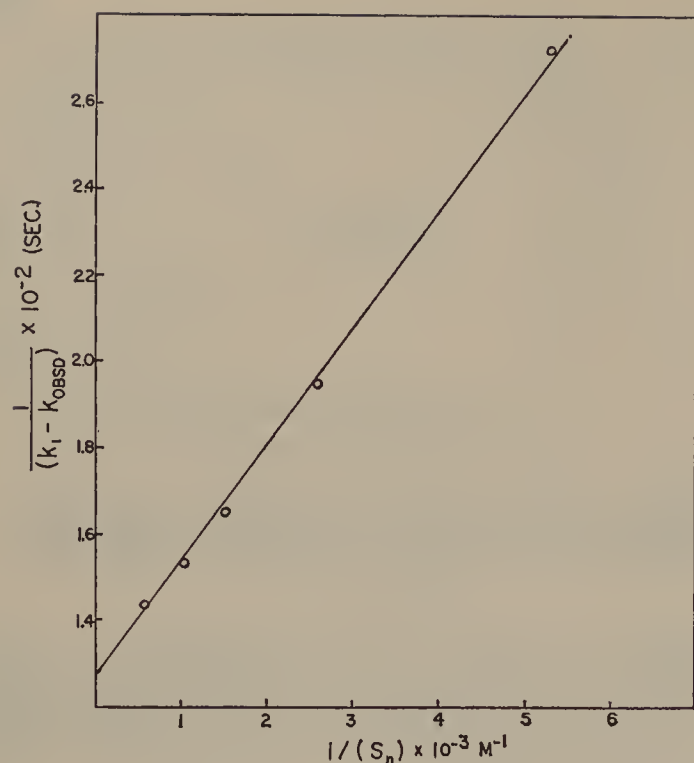
Figure 6. The determination of the rate constant for hydrolysis of adsorbed mono-p-nitrophenyl dodecanedioate. See eq 3 and accompanying text.

micellar material. Thus, the scheme shown in eq 1 is proposed in which S_n, E, and S_nE represent micellar surfactant, free ester, and adsorbed ester, respectively.[29] In order to evaluate the micelle concentration we make use of the "phase-separation" concept which assumes that the unassociated surfactant concentration remains

$$S_n + E \underset{k_1}{\overset{K}{\rightleftarrows}} S_nE \quad\quad (1)$$
$$\downarrow k_1 \quad\quad \downarrow k_2$$
$$P \quad\quad\quad P$$
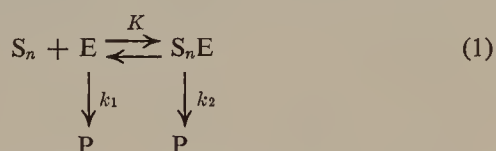
constant above the CMC. (This assumption has experimental support[30] and greatly simplifies matters here, but it also has limitations.)[31] If the average number of molecules per laurate micelle is 33,[32] then the micelle concentration is approximated by eq 2 where

$$(S_n) = \frac{(\text{laurate})_t - \text{CMC}}{33} \quad\quad (2)$$

(laurate)$_t$ signifies the total concentration of laurate. The rate constant for hydrolysis of adsorbed substrate, k_2, can now be determined from eq 3[33] by plotting

$$\frac{1}{(k_1 - k_{obsd})} = \frac{1}{(k_1 - k_2)} + \frac{1}{(k_1 - k_2)K(S_n)} \quad\quad (3)$$

$1/(k_1 - k_{obsd})$ vs. $1/(S_n)$ using measured values of k_1 and k_{obsd} (the rate constants for ester hydrolysis in the absence and presence of surfactant such as given in Table I). Such a plot for substrate B (mono-p-nitrophenyl dodecanedioate) is presented in Figure 6. Its linearity is remarkable in view of the assumptions made

(29) See A. K. Colter, S. S. Wang, G. H. Megerle, and P. S. Ossip, *J. Am. Chem. Soc.*, **86**, 3106 (1964), for a similar scheme describing a nonmicellar system.

(30) (a) K. Shinoda and E. Hutchinson, *J. Phys. Chem.*, **66**, 557 (1962); (b) J. T. Yang and J. F. Foster, *ibid.*, **57**, 628 (1953).

(31) M. Abu-Hamdiyyah and K. J. Mysels, *ibid.*, **71**, 418 (1967).

(32) Reference 3a, p 67.

(33) Equation 3 holds only for those runs in which $(S_n) >$ (substrate), that is, where (laurate)$_t >$ CMC.

in this analysis: (a) substrate does not complex with surfactant monomer; (b) substrate does not perturb micellation; (c) substrate associates with the micelles in a 1:1 stoichiometry; (d) micellation occurs exactly at the CMC rather than over a small concentration range; (e) eq 2 is valid.

Since the intercepts of the reciprocal plots for substrates A and B are within the experimental error of $1/k_1$, the rate of hydrolysis of these substrates when adsorbed into the micelles must be zero![34] Application of eq 3 to substrate C fails because K is too large for an accurate plot, but clearly micellar C is also unreactive since 0.03 M laurate reduces the hydrolysis rate to less than 3% of that in the absence of surfactant. The only reason that surfactant affects the rate of hydrolysis of p-nitrophenyl acetate (A) less than the other substrates (Figure 1) is that partitioning of A into the micellar phase from the solvent is less favorable.

The remarkable rate inhibitions may be explained by ester adsorption into the hydrocarbon center of the micelles where presumably there is no anionic nucleophile. Alternatively, adsorption could occur within the outer aqueous areas of the micelles where the hydroxide ion concentration might be greatly reduced because of electrostatic factors originating at the micelle surface. We favor the former rationale for two reasons. First of all, substrate B is ionic; this means that one end of the adsorbed molecule is in the aqueous region of the micelle. The ester moiety, many carbons away from the ionic end, must then be directed toward the center of the micelle (unless B forms a loop within the aggregate). Indeed, substrate B was selected for study because it was considered a useful compound for examining the properties of the inner regions of micelles. Second, while it is conceivable that there is a lowered hydroxide ion concentration in the aqueous portion of the micelles, there still remains a very high concentration of another nucleophile, carboxylate anion. Intramolecular carboxylate catalysis of ester hydrolyses can lead to enormous rate increases,[35] suggesting that the ester sites are not very near the micelle surface. This seems to be true even for a cationic substrate, benzoylcholine (D; Figure 5A).

It is possible to evaluate the association constant for micelle–substrate interaction (K) from eq 3. The value of K, defined as $(S_nE)/(S_n)(E)$, for substrate B is 4.5×10^3 M^{-1}. Laurate micelles thus bind B better than α-chymotrypsin binds many of its specific substrates. The truly sizeable association constant is further evidence of internal adsorption as it is difficult to imagine why surface adsorption would be so efficient.

The effect of n-dodecyltrimethylammonium ion (F) on the hydrolyses of the four substrates can be seen in Figures 3 and 5B. The hydrolysis rates of the long-chain substrates B and C decrease with increasing surfactant in the region above the CMC. Partitioning of the esters into the hydrocarbon interior of the micelles seems to be occurring much like it does in the laurate system. The substrate–micelle association constants for anionic B and neutral C are similar in the cationic soap solutions, whereas laurate micelles bind B less ef-

(34) It is interesting that surfactants can significantly inhibit *unimolecular* light-induced reactions as well: F. M. Menger, S. P. Pappas, and R. Gresham, unpublished observations.

(35) T. C. Bruice and U. K. Pandit, *J. Am. Chem. Soc.*, **82**, 3386 (1960).

fectively than C (Figure 1). This is not surprising; the anionic end of B can be readily included within the electrical double layer of surfactant F micelles. Since B is more water soluble than C, it is clear that the affinity of n-dodecyltrimethylammonium ion micelles for B is in reality larger than for C. The small substrate A shows a modest rate increase above the CMC, which is consistent with inclusion of the ester within the outer aqueous portion of the micelle interior or else directly on the micelle surface. An interesting feature of Figure 3 is that the hydrolysis rates of the long-chain esters are enhanced *below* the CMC, while *p*-nitrophenyl acetate is not affected in this concentration range. The rate of basic hydrolysis of benzylideneacetophenone also increases in a cationic surfactant solution below the CMC.[4] This was explained by association of the Schiff base with one or more surfactant molecules to form a positively charged complex which reacts readily with hydroxide ion. Our findings are in agreement with this rationale since the only substrates which display pre-CMC rate perturbations are ones which possess large hydrocarbon moieties that can hydrophobically bind to surfactant. Perhaps the small rate drop below the CMC in Figure 1C is also caused by nonmicellar complexation.

n-Dodecylpyridinium ion (G) has either a small effect (Figure 4A) or no effect at all (Figures 4B and 4C) on the esters. Therefore, k_1 is nearly equal to k_2 (eq 1) or else there is little substrate adsorption (K is a small number). Some complexation is taking place because the solubilities of esters B and C are increased in the presence of n-dodecylpyridinium ion micelles. We conjecture that, because of the bulk and flatness of the surfactant "heads," the micelles are unusually loose structures containing considerable amounts of water. Association constants and rate perturbations are consequently not large. In any event the properties of solutions of n-dodecylpyridinium ion and n-dodecyltrimethylammonium ion are appreciably different despite the structural similarity of the surfactants.

A great deal remains to be learned about the effect of micellation upon reaction rates. In addition, virtually nothing is known about how surfactants affect the stereochemistry and product distribution of thermal and photochemical reactions. These important aspects of molecular aggregate chemistry are also currently under investigation in these laboratories.

Aggregation of Metallochlorophylls[1]

L. J. Boucher[2] and Joseph J. Katz

Contribution from the Chemistry Division, Argonne National Laboratory, Argonne, Illinois 60439. Received April 21, 1967

Abstract: The self-aggregation of divalent nickel, copper, and zinc methyl pheophorbides a and b has been examined by infrared spectroscopy. Of these, only the zinc compounds show significant coordination aggregation. Nmr measurements on zinc pheophytin a and zinc methyl pheophorbide a and b show that both coordination aggregation and $\pi-\pi$ aggregation occur in nonpolar solvents. Nmr and infrared measurements indicate that under comparable conditions in nonpolar solvents the zinc chlorophylls are aggregated to a considerably lesser extent than are the magnesium chlorophylls. Visible and infrared spectra of nickel, copper, and zinc methyl pheophorbides a and b are reported, and tentative band assignments are made. Considerations of absorption position and relative intensities suggest that the extent of metal–ligand interaction follows the order: Ni > Cu > Zn > Mg.

Metal ions play a decisive but little understood role in the photosynthetic unit. For example, the most important compound of photosynthesis, chlorophyll, is a magnesium(II) complex of a dihydroporphyrin (chlorin) ligand. Examination of chlorophyll derivatives in which magnesium is replaced by other metal ions (metallochlorophylls) are valuable in that they provide information about the contribution of the metal to the various properties and functions of chlorophyll. The state of aggregation of chlorophyll is one property in particular that is a subject of keen interest today.[3] Association of chlorophyll molecules in solution can occur in a number of ways. One mechanism, designated coordination aggregation, involves the intermolecular coordination of the ketone oxygen of one chlorophyll molecule to a magnesium atom in another molecule.[4] An important question then is: is coordination aggregation a unique property of magnesium-containing chlorophylls, or do other metallochlorophylls show similar behavior? The aggregation properties of metallochlorophylls in solution appear not to have been previously studied.

This paper presents some new information derived from infrared and nmr measurements on the aggregation behavior of divalent nickel, copper, and zinc chlorophylls. The structural formulas, nomenclature, and proton numbering of the materials studied are given

(1) Based on work performed under the auspices of the U. S. Atomic Energy Commission.
(2) Resident Research Associate, 1964–1966.
(3) See, for example, J. J. Katz, R. C. Dougherty, and L. J. Boucher in "The Chlorophylls," L. P. Vernon and G. R. Seely, Ed., Academic Press Inc., New York, N. Y., 1966, p 186.

(4) J. J. Katz, G. L. Closs, F. C. Pennington, M. R. Thomas, and H. H. Strain, *J. Am. Chem. Soc.*, **85**, 3801 (1963).

Figure 1. Structure, nomenclature, and proton designation of metallochlorophylls. * Referred to in the text either as zinc pheophytin or zinc chlorophyll.

No.	Ligand	M	R	Proton No. of R	R'
Ia	Pheophytin*	Zn	CH₃	3a	Phytyl
IIa	Methyl pheophorbide a	Zn	CH₃	3a	CH₃
IIIa	Methyl pheophorbide a	Cu	CH₃	3a	CH₃
IVa	Methyl pheophorbide a	Ni	CH₃	3a	CH₃
IIb	Methyl pheophorbide b	Zn	CHO	3b	CH₃
IIIb	Methyl pheophorbide b	Cu	CHO	3b	CH₃
IVb	Methyl pheophorbide b	Ni	CHO	3b	CH₃

Figure 2. Visible spectrum of zinc methyl pheophorbide a in chloroform.

in Figure 1. Nomenclature for the metal derivatives of the methyl pheophorbides and pheophytins is quite straightforward. However, the naturally occurring magnesium derivative of pheophytin is often called magnesium chlorophyll, and so we find ourselves referring to zinc and the other metal pheophytins (Figure 1) also as zinc, nickel, or copper chlorophyll when it is important to emphasize the relation to natural chlorophyll. All the metal derivatives of the pheophytins and methyl pheophorbides are simply designated metallochlorophylls.

Experimental Section

Materials. Methyl pheophorbide a and pheophytin a were prepared from chlorophyll a by standard procedures.[5] Methyl pheophorbide b was obtained from Fluka A.G. Chemische Fabrik Buchs/S. G., Switzerland. Methyl chlorophyllides a and b were prepared from cockleburr by the *in situ* reaction with methanol.[6] All other chemicals were reagent grade and were used without further purification. Destabilized chloroform was prepared by washing commercial chloroform with water several times to remove ethanol and then drying over Drierite.

Preparation of Complexes. The compounds were prepared by standard procedures.[5] The ligand (~50 mg) dissolved in chloroform and a fivefold excess of the metal acetate dissolved in methanol were refluxed for 30 min in dim light under a nitrogen blanket. The rate of formation of complex is so slow that the nickel complexes cannot be conveniently prepared with the chloroform–methanol solvent system. A chloroform–glacial acetic acid mixture and a reaction time of 1 hr proved satisfactory in this case. The cooled reaction mixture was then washed several times with water to remove unreacted metal salts. The chloroform solution of the reaction mixture was evaporated to dryness and the residue was extracted with benzene. The benzene solution was adsorbed on a dry packed sucrose column (5 × 30 mm) and eluted with benzene and 0.1% 1-propanol–benzene mixture. Usually four green fractions were collected, and a small dark green zone remained adsorbed on top of the column. The second fraction, which contains the desired product, was then washed with water to remove any

dissolved sucrose and dried. The volume of the solution was reduced and a green solid was precipitated by addition of petroleum ether (bp 30–60°). Thin layer chromatography on silica gel G generally showed traces of fractions one and three in addition to the metallochlorophyll. The impure solid was then rechromatographed on sucrose until tlc indicated only one component. The pure green solid was dried by repeatedly dissolving in carbon tetrachloride and then removing the solvent on the vacuum line. The dried solids were stored in the dark in evacuated containers. The yield of pure product was around 50% for the copper and zinc and about 20% for the nickel complexes.

Spectroscopic evidence indicates that fraction 3 from column chromatography contained the unreacted ligand. Absorption spectra of fractions 1 and 4 showed a 10–15-mμ blue shift of the absorption bands and a doubling of the relative intensity of the blue band, as compared to the metallochlorophylls. Further, infrared spectra show no ketone carbonyl absorption. These data indicate that these materials are metal complexes of altered chlorophylls. The altered chlorophylls probably are of the chlorin type with a ruptured ring V.[7]

The materials used in this study were chromatographically pure, and their visible, ultraviolet, infrared, and nmr spectra are entirely compatible with their presumed molecular structures.

Spectral Measurements. Absorption spectra were recorded with a Cary Model 14 spectrophotometer on chloroform solutions of the materials in 1-cm silica cells. Infrared spectra of the complexes were recorded with Beckman IR-7 and IR-12 spectrophotometers. Solid-state spectra were taken with the materials in potassium bromide disks and checked with Nujol mulls. Solution spectra (0.05 M) were taken in 0.1-mm sodium chloride cells. Nmr spectra were recorded on a Varian HA-100 nmr spectrometer in the field-sweep mode. Chemical shifts are measured from hexamethyldisiloxane, with chemical shifts to lower fields positive. The compounds were dissolved in CDCl₃ or tetrahydrofuran-d_8 to which 10% HMS was added. The solutions were then sealed in nmr tubes under vacuum after being degassed several times. A Mechrolab vapor pressure osmometer Model 301A was used to determine molecular weights of the substances in chloroform by procedures essentially the same as previously described.[4]

Results and Discussion

Spectral Properties. A typical electronic spectrum is shown in Figure 2, and the positions of the absorption maxima for the methyl pheophorbide complexes are presented in Table I. Data for the magnesium(II) complex (methyl chlorophyllides) are included for comparison. The spectra show a strong absorption band in the red (I) and a usually more intense absorption in the blue (V). Three much weaker bands (II–IV) appear between these two and are difficult to place accurately. In some of the spectra a prominent shoulder appears on the high-energy side of the blue

(5) H. Fischer and H. Orth, "Die Chemie des Pyrrols," Vol. II, Part 2, Akademische Verlgsgesellschaft, Leipzig, 1940.

(6) F. C. Pennington, H. H. Strain, W. A. Svec, and J. J. Katz, *J. Am. Chem. Soc.*, **86**, 1418 (1964).

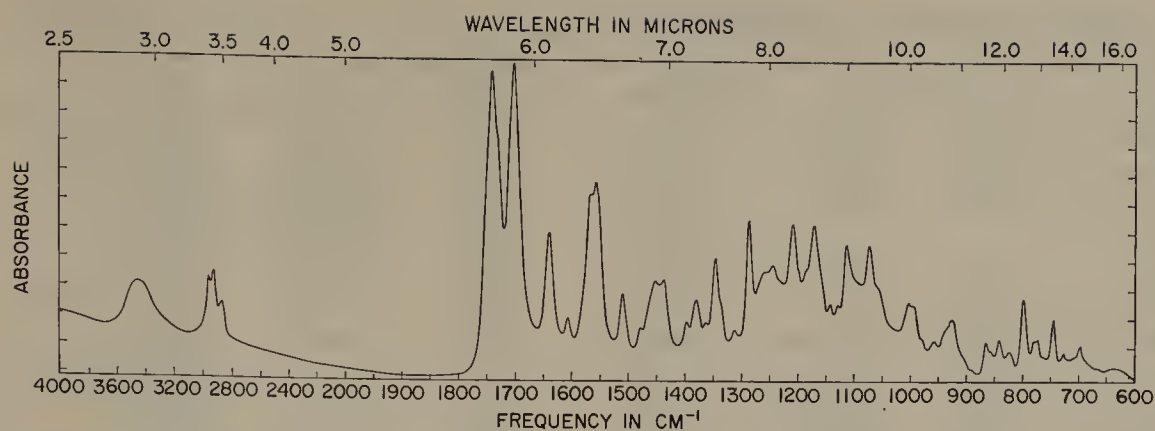(7) H. H. Inhoffen, G. Klotmann, and G. Jeckel, *Ann.*, **695**, 112 (1966).

Figure 3. Infrared spectrum of copper methyl pheophorbide a in potassium bromide pellet.

band. The absorption spectra are similar to those of the chlorophylls[8] and consistent with the proposed structure of the metallochlorophylls.

Table I. Absorption Maxima of Metallochlorophylls

| Complex | Peaks, $m\mu$ | | | | | | $A\nu/A_I$ |
	I	II	III	IV	V	VI	
	Methyl pheophorbide a						
Mg	664	617	574	532	432	415	1.31
Zn	658	608	556	514	426	408	1.30
Cu	654	608	546	505	425	399	1.18
Ni	652	608	539	494	423	394	0.95
	Methyl pheophorbide b						
Mg	647	598	570	545	458	437	2.67
Zn	638	593	564	540	448		2.61
Cu	633	587	556	522	444		2.31
Ni	632	593	553	516	430		1.93

Two pieces of information that can be obtained from the spectra are of immediate interest. One is the position of the maximum, particularly of the red and blue bands, and the other is the relative intensities of these bands. The λ_{max} of the red and blue bands move to higher energy in the order Ni > Cu > Zn > Mg. The shifts for the methyl pheophorbide a complexes are somewhat less than for the methyl pheophorbide b complexes. Ratios of the absorbances of the blue and red bands are given in the last column of Table I. The ratio varies for the series of compounds with Ni < Cu < Zn ≤ Mg. Finally, the ratio for the methyl pheophorbide a complexes are considerably less than for the methyl pheophorbide b complexes.

A typical infrared spectrum is shown in Figure 3. The frequencies of the prominent absorption peaks for the methyl pheophorbide a and b complexes in the 4000–650-cm^{-1} region are collected in Table II. Data for the methyl chlorophyllides are again listed for comparison. The assignments given in Table II follow those given previously for the chlorophylls[3] and metalloporphyrins.[9] The infrared spectra obtained are entirely consistent with the proposed structures of the metallochlorophylls. Most of the ligand absorption positions are more or less independent of the metal ion. On the other hand, C–C and C–N stretching absorptions of the chlorin macrocycle are sensitive to the particular metal ion present. The complexes show two prominent medium-intensity absorptions in the 1500–1700-cm^{-1} region. The frequency of the bands at 1670–1600 cm^{-1}

and 1585–1535 cm^{-1} is in the order: Ni > Cu > Zn > Mg. The relative intensity of the macrocycle stretching vibration and metal ion dependence of the frequency are greater for the chlorophylls than for the corresponding metalloporphyrins.[9] Far-infrared spectra of the copper chlorophylls show the strongest absorption below 650 cm^{-1} at 304 cm^{-1}. This band is absent from the spectra of the metal-free ligand and probably arises from a copper–ligand vibration.[10] This absorption band is at a higher frequency for the metallochlorophylls, which may be interpreted to indicate a greater stability for the copper complex than for the magnesium complex.

The electronic and vibration spectra vary considerably in the series of metallochlorophylls. Frequency shifts and relative intensity variation give rise to the order: Ni > Cu > Zn > Mg. Spectroscopic evidence leads to an identical order for the metalloporphyrins.[11] The chemical stability of the metal–ligand linkage also varies in a similar way for the metalloporphyrins. It is not unreasonable to suppose that the stability of the metal–ligand band is related in the same way to the spectroscopic order for the metallochlorophylls. Unfortunately, no thorough study of the stability of the metallochlorophylls has as yet been carried out. Bearing on this point is the report that zinc chlorophyll is more stable to acid demetalization than is the magnesium compound[12a] and that the stability of metallochlorophylls to photochemical decomposition is in the order Cu > Zn > Mg.[12b]

Aggregation Properties. Examination of the solvent dependence of the carbonyl region (1750–1600 cm^{-1}) infrared absorption can furnish useful information about the coordination aggregation of chlorophyll compounds.[4] In nonpolar solvents, and in the solid, chlorophyll a exists primarily in the aggregated state. The C-9 ketone absorption appears as two peaks: one is the normal ketone absorption at $\sim$1700 cm^{-1}; the other, originating in the ketone oxygen coordinated to magnesium, occurs at somewhat lower frequency ($\sim$1650 cm^{-1}). The latter may properly be termed an aggregation peak, and its occurrence in an infrared spectrum is a valid diagnosis for the presence of chlorophyll-like aggregates. In polar solvents such as tetra-

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Table II. Infrared Absorption Bands (cm^{-1}) in Metallochlorophylls[a]

Mg	Zn	Cu	Ni	Mg	Zn	Cu	Ni	Assignment
	Methyl pheophorbide a				Methyl pheophorbide b			
2955 w	2960 w	2955 w	2955 w	2960 w	2950 w	2960 w	2955 w	ν(C–H)
2935 w	2930 w	2930 w	2925 w	2925 w	2925 w	2930 w	2930 w	
2870 w	2865 w	2860 w	2860 w	2860 w	2865 w	2870 w	2870 w	
				2750 w	2750 w	2740 w	2740 w	Aldehyde
1736 s	1739 s	1741 s	1742 s	1735 s	1740 s	1743 s	1741 s	Ester
1696 s	1693 s	1704 s	1707 s	1696 s	1708 s	1710 s	1712 s	Ketone ν(C=O)
				1658 m	1663 m	1668 m	1665 s	Aldehyde
1607 m	1617 m	1638 m	1661 m	1603 m	1616 m	1642 m	1665 s	
	1607 w		1632 w				1612 w	ν(ring)
1547 m	1552 w	1556 m	1576 m	1544 s	1556 s	1572 m	1585 m	
1531 w	1539 m	1510 w	1521 w	1517 w		1504 w	1516 w	
1486 w	1498 w	1480 w	1480 w	1474 w	1489 w	1468 w	1484 w	
1457 w	1450 w	1451 w	1452 w	1441 w	1449 w	1455 w	1452 w	
1449 w	1439 w	1437 w	1437 w			1439 w	1438 w	
1373 w	1378 w	1370 w	1382 w	1376 w	1380 w	1382 w	1380 w	
1340 w	1347 w	1345 w	1347 w	1343 w	1349 w	1349 w	1348 w	
1281 m	1288 m	1286 m	1283 w	1284 m	1292 m	1289 m	1287 m	
1252 w	1240 w	1245 w	1244 w		1242 w	1238 w	1239 w	
1194 w	1189 w	1208 w	1214 w	1189 w	1211 w	1218 w		
1162 w	1160 w	1170 w	1169 w	1166 w	1169 w	1170 w	1169 w	ν(C–O) Ester
1134 w	1134 w			1143 w	1138 w	1132 w	1134 w	
1086 w		1112 w	1108 w	1083 w		1107 w	1108 w	
1064 w	1069 w	1073 w	1076 w	1062 w	1066 w	1070 w	1073 w	
1049 w	1042 w			1038 w	1048 w	1051 w	1052 w	
984 w	991 w	1003 w	1002 w	1002 w	1005 w	1008 w	1014 w	
914 w	920 w	926 w	939 w	921 w	928 w	942 w	946 w	
839 w	846 w	841 w	842 w	839 w	833 w	837 w	843 w	
799 w	797 w	798 w	798 w	799 w	798 w	801 w	798 w	π(C–H) Meso
780 w	764 w	775 w	764 w	758 w	758 w	759 w	759 w	
748 w	742 w	743 w	747 w	737 w	736 w	740 w	743 w	
693 w	709 w	695 w	697 w	702 w	704 w	704 w	705 w	

[a] Potassium bromide pellets; s = strong, m = medium, w = weak.

hydrofuran, chlorophyll exists primarily in monomeric form; the aggregation peak is completely absent from the carbonyl region spectrum.

The infrared spectra of the metallochlorophylls both in solution and in the solid form were examined. Typical spectra for zinc pheophytin a are given in Figure 4. In nonpolar solvents, such as carbon tetrachloride and chloroform, and in the solid, an aggregation peak is easily seen at 1660–1655 cm^{-1}. The spectra in polar solvents on the other hand do not show an aggregation peak. Zinc methyl pheophorbide a exhibits a similar behavior. Here the aggregation peak is much more intense for the carbon tetrachloride solution than for a destabilized chloroform solution or for the substance in the solid state. For chlorophyll b, both the aldehyde and ketone carbonyl oxygens participate in aggregate formation by coordination to the metal, and these provide two sources of aggregation peaks in the infrared at 1660 and 1610 cm^{-1}. Thus, for the aggregated species in nonpolar solvents: (1) the peak near 1660 cm^{-1} is partially due to the aggregation (ketone) peak and partially to the free aldehyde; (2) the peak near 1610 cm^{-1} is partially due to the ring vibration but also contains a contribution from an aldehyde aggregation peak.[4] The relative intensities of the bands (1700–1600 cm^{-1}) in polar and nonpolar solvents support this interpretation of the chlorophyll b infrared spectra. For zinc methyl pheophorbide b the carbonyl region spectrum shows solvent dependence, which is consistent with aggregation in nonpolar solvents and in the solid. The relative intensity of the free ketone absorption is less, while that of the peak near 1610 cm^{-1} is greater in carbon tetrachloride than in tetrahydrofuran. Molecular weight measurements of zinc methyl pheophorbide

b are informative, as the assessment of the extent of aggregation from the infrared spectra is not entirely straightforward. Solutions of zinc methyl pheophorbide b in destabilized chloroform with a calculated molarity of 0.040 and 0.020 M have an observed molarity of 0.025 and 0.012 M, and this is clearly indicative of substantial aggregation in these solvents.

There is no evidence from the infrared spectra to indicate coordination aggregation for either nickel or copper methyl pheophorbide a or b, and the carbonyl region spectra of these compounds show no solvent dependence. The spectra, in fact, are identical in nonpolar solvents, in the solid state, and in polar solvents. The far-infrared spectra of copper chlorophylls also show no solvent dependence.

Proton magnetic resonance measurements on solutions of the zinc chlorophylls likewise yield information about the state of aggregation of these substances. In chloroform, the nmr spectra are poorly resolved. In tetrahydrofuran solution, the spectra become sharp, and a number of the proton resonance signals are observed to show changes in chemical shifts. These solvent-dependent shifts are particularly noticeable in the methyl and methine resonance regions and in the behavior of the C-10 proton signal. Nmr data are summarized in Table III. Chemical shift assignments are based on previous assignments of the nmr spectra of the chlorophylls.[13] The nmr spectra of the zinc chlorophylls in tetrahydrofuran, it may again be noted, are entirely consistent with the proposed structure of the materials.

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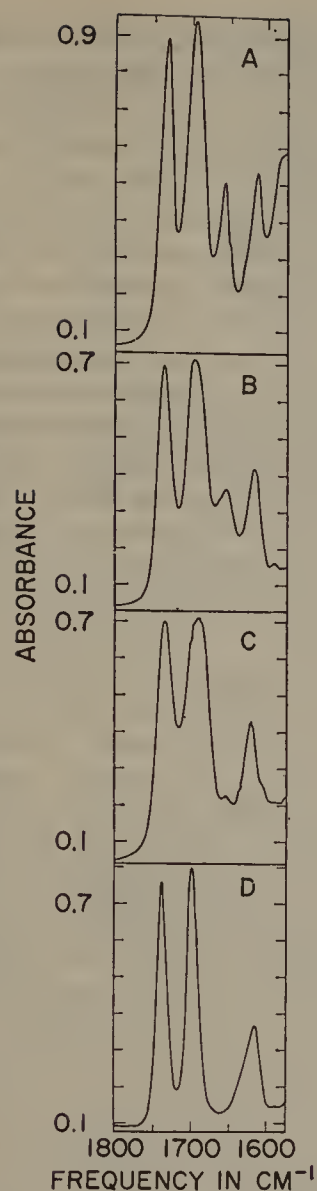
Figure 4. Infrared spectra of zinc pheophytin a: (A) in carbon tetrachloride; (B) in destabilized chloroform; (C) in potassium bromide pellet; (D) in tetrahydrofuran.

Figure 5. Nmr dilution shifts of zinc pheophytin a in deuterio-chloroform.

The large paramagnetic shifts experienced by some of the proton resonance in nonpolar solvents can be attributed mainly to specific solute–solute interactions.[13] In chloroform the zinc chlorophylls are aggregated and

Table III. Chemical Shifts for Zinc Chlorophylls Dissolved in $CDCl_3$ (A) and THF-d_8 (B)[b]

Pro-ton[c]	δ, ppm[a] Ia		IIa		IIb	
	A	B	A	B	A	B
α	8.46	9.24	8.64	9.17	9.22	10.15
β	8.78	9.51	8.92	9.40	9.07	9.58
δ	8.24	8.46	8.27	8.38	8.22	8.44
10	5.42	6.07	5.64	6.08	4.93	6.12
11	3.66	3.68	3.70	3.75	3.53	3.58
5	3.15	3.54	3.24	3.48	3.19	3.45
1	3.11	3.26	3.15	3.28	3.15	3.18
3a	2.55	3.14	2.69	3.15		
3b					9.12	11.06

[a] From hexamethyldisiloxane. [b] Concentrations: Ia, 0.08 M; IIa and IIb, 0.06 M. [c] Proton numbering and compound designation are given in Figure 1.

in tetrahydrofuran the materials are monomeric (disaggregated). The observed solvent dependence of the nmr spectra entirely parallels the solvent dependence of the infrared spectra. In the aggregated form, protons

in regions of the molecule that involve mutual overlap are expected to be highly shielded. In fact, aggregates of the zinc chlorophylls appear to have two highly shielded regions: (1) in the region of ring II for the α, β, and 3a (3b) protons; (2) in the region of ring V and the ketone carbonyl as deduced from the behavior of the 5, 10, and 11 protons. The first region coincides with what is observed for the $\pi-\pi$ aggregation of the metal-free methyl pheophorbide. The relatively large shifts of the aldehyde protons may also indicate that the aldehyde oxygen is involved in coordination aggregation. The second region of mutual overlap in the aggregates is consistent with coordination aggregation.[3] However, the small change in chemical shift of the C-11 protons as the aggregate is dissociated to monomer may indicate that the extent of coordination aggregation is not large. At any rate, the nmr spectra are consistent with the idea that two kinds of aggregates exist in nonpolar solution of the zinc chlorophylls.

The change of chemical shift values with dilution of chloroform solutions of zinc pheophytin a is shown in Figure 5. The extent to which aggregated species occur in solution is strongly concentration dependent. From the maximum concentration to about 0.05 M the chemical shift values for the 11, 10, and 5 protons appear to be independent of concentration. On the other hand, the α and 3a protons, and to a lesser extent the β proton, show chemical shifts that vary significantly with concentration. The $\pi-\pi$ aggregation of the metal-free methyl pheophorbides is also strongly concentration

dependent, with the α, 3a, and β proton chemical shift values varying in a similar way as for the zinc compounds. Coordination aggregation of the chlorophylls, however, is not concentration dependent in this concentration range. Below 0.5 M for zinc pheophytin a, the chemical shift values of the α, 3a, β, 10, and 5 protons are all clearly concentration dependent. In the high concentration range only the π–π aggregates dissociate appreciably, while in the lower concentration range both the π–π and the coordination aggregates are dissociating. Since only one set of lines exists for the protons in the aggregated solution, labile equilibrium must exist among the two types of aggregates and the monomeric unit.

The solvent dependence of the infrared spectra show that the only metallochlorophylls that undergo significant coordination aggregation are the zinc complexes. Copper and nickel methyl pheophorbides, mercury and cadmium pheophytin a, and silver pyropheophytin[14] do not undergo aggregation via the coordination mechanism. Metallochlorophylls, like metalloporphyrins, undoubtedly experience π–π aggregation in nonpolar solvents. Recent esr spectral evidence[15] indicates that copper and silver methylpyropheophorbides a form π–π aggregates. The nmr dilution shift measurements for zinc pheophytin a also testify to the importance of this type of aggregation in metallochlorophylls.

The relative intensity of the infrared aggregation peak for the zinc chlorophylls in the most favorable solvent is only about one-third that for chlorophyll itself. The concentration dependence of the chemical shift values for zinc pheophytin a is consistent with the substantial dissociation of the coordination aggregates in the concentration range near 0.02 M. At this and lower concentrations, chlorophyll aggregates are virtually undissociated. These data thus indicate that the stability of the zinc chlorophyll aggregates is much lower than the magnesium-containing chlorophylls under similar conditions. In fact, the zinc chlorophyll coordination aggregates are quite likely not much more stable than their π–π aggregates. Further, the zinc chlorophylls appear to be (from infrared) only slightly aggregated in the solid state, whereas coordination aggregation appears to be an important crystal-forming force in the chlorophylls.[16] Infrared measurements on chlorophylls show a greater extent of aggregation in the solid phase than in solution. It can be concluded from these observations that strength of the zinc–oxygen interaction is not great enough to stabilize a particular structure in the crystal. Relevant is the report that only magnesium, and to a lesser extent zinc, chlorophylls form colloids in dioxane–water mixtures,[17] while cobalt, nickel, and copper chlorophylls do not to any significant extent.

The ability of the magnesium and zinc chlorophylls to form coordination aggregates agrees closely with the ability of these compounds to add a fifth (axial) ligand. Magnesium and zinc chlorophylls (and porphyrins) readily add ligand, while the copper and nickel complexes do not.[18] The differences between the magnesium and zinc chlorophylls may be rationalized by considering the result of a molecular orbital calculation on metalloporphyrins which shows positive charge on the metal to be 0.57 for magnesium and 0.40 for zinc.[19] The higher positive charge makes the electrostatic interaction with the ketone oxygen involved in aggregated formation more favorable for the magnesium compounds than for the zinc compounds, and to a certain extent this difference in charge accounts for the differences in aggregation properties and perhaps for other important properties as well.

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Solvent Effects in Reactions of Amino Groups in Amino Acids, Peptides, and Proteins with α,β-Unsaturated Compounds[1]

Mendel Friedman

Contribution from the Northern Regional Research Laboratory,[2] Peoria, Illinois 61604. Received February 15, 1967

Abstract: The reaction rates of amino groups in structurally different amino acids, peptides, and proteins with α,β-unsaturated compounds were studied in a medium consisting of 50% pH 8.4 buffer–50% dimethyl sulfoxide (DMSO) and were compared to analogous rates in an aqueous buffer. The presence of DMSO in the aqueous buffer resulted in a variable rate enhancement directly related to the pK_2 values of the amino groups. A plot of the logarithm of the ratio of second-order rate constants determined in the mixed solvent system to that in the aqueous buffer *vs.* pK_2 is linear. The straight line is described by the relationship $R = 0.855pK_2 - 6.505$. Rates in the mixed solvent system are more sensitive to changes in basicities of amino groups than corresponding rates determined in aqueous buffers. Additional studies were carried out on the influence of several variables on rates. The results are rationalized in terms of participation of aprotic solvents in acid–base equilibria, stabilization of ground and transition states, and hydrogen-bonding interactions. The configuration and conformation of a protein appear to be significant in governing relative reactivities of its amino groups.

Dipolar aprotic solvents, like dimethyl sulfoxide (DMSO), are known to accelerate a number of organic reactions, presumably because they are able to solvate cations preferentially and thus free the anion from the destabilizing influence of a positive charge and ion-pair aggregation.[3-6] Such a mechanism of catalysis by dipolar solvents explains the large rate-enhancing effect of these solvents in nucleophilic displacement reactions in which negatively charged nucleophiles participate. Although amino acid anions of structure NH_2RCOO^- are negatively charged nucleophiles, the negative charge is not located on the amino group that is involved in nucleophilic displacement and addition reactions. It was therefore of theoretical interest to establish the influence of nonaqueous solvents on reaction rates of these unique nucleophilic species.

The reaction selected for this study is a Michael-type nucleophilic addition as illustrated by glycine and acrylonitrile

$$^-OOCCH_2\overset{+}{N}H_3 + B \xrightleftharpoons{K_2} {}^-OOCCH_2NH_2 + BH^+ \quad (1)$$
$$\text{I} \qquad\qquad\qquad\qquad \text{II}$$

$$^-OOCCH_2NH_2 + CH_2{=}CHCN \longrightarrow$$
$$\text{II} \qquad\qquad \text{III}$$

$$^-OOCCH_2\overset{+}{N}H_2{-}CH_2{-}\bar{C}HCN \quad (2)$$
$$\text{IV}$$
$$\downarrow$$
$$^-OOCCH_2NHCH_2CH_2CN$$
$$\text{V}$$
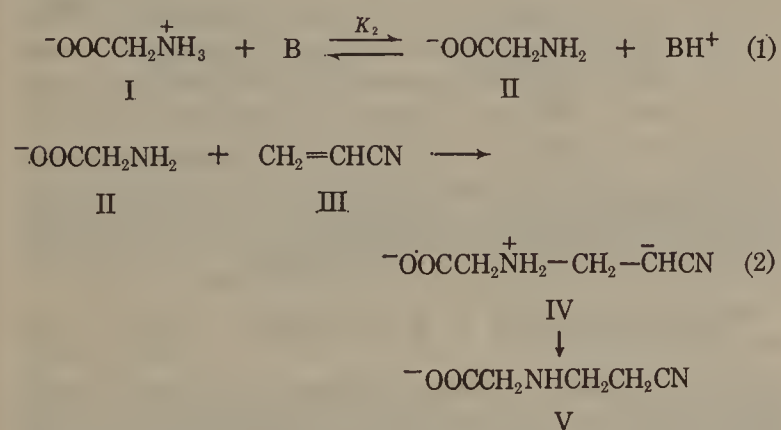
A base removes a proton from zwitterion I to give the anion II, which then reacts in the rate-determining step with acrylonitrile III.

In previous communications in this series, studies are described on the nature of parameters that govern reactivities of functional groups present in proteins with α,β-unsaturated compounds[7-11] and with ninhydrin.[12] Linear free-energy relationships were developed which correlate the observed results in terms of polar, steric, and nucleophilic parameters associated with each of the reactants.

The latest study was designed to determine the relative influence of nonaqueous solvents on reaction rates of amino groups with α,β-unsaturated compounds to delineate the mechanism of interaction of these solvents with ground and transition states. Reaction rates of amino groups in structurally different amino acids, peptides, and proteins were studied in media consisting of mixtures of nonaqueous solvents and aqueous buffers. The observed rates were compared to analogous rates determined in the aqueous buffers.

To gain some insight into the mechanism of the solvent effects at a molecular level, a number of variables were investigated. These include steric environment and basicities of the amino groups, nature of the vinyl compounds, nature of the solvent, pH of the aqueous buffer, and concentration of dimethyl sulfoxide. The observed results are explained in terms of solvation mechanisms responsible for the increased basicities and nucleophilicities of the amino groups in the ground state and for better stabilization of the transition states. Evidence indicates that dimethyl sulfoxide affects hydrogen-bonding interactions which influence rates.

Results and Discussion

Effect of Basicities of Amino Groups on Rates.
Rates of reaction were followed by the ninhydrin colorimetric procedure previously described,[7] which measures the

(1) Presented at the 152nd National Meeting of the American Chemical Society, New York, N. Y., Sept 11–16, 1966, Abstracts, p C45. This is part VIII in a series on "Reactions of Amino Acids, Peptides, and Proteins with α,β-Unsaturated Compounds." For part VII, see L. H. Krull and M. Friedman, *J. Polymer Sci.*, in press.

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Table I. Rates of Reaction with Acrylonitrile at 30° as a Function of pK_2 Values of Amino Groups (units for all rate constants are in l./mole sec)

No.	Amino compd	$pK_2{}^a$	$k_A{}^{-a} \times 10^4$	$k_2{}^a \times 10^4$, pH 8.4 (A)	$k_2 \times 10^4$, 50% pH 8.4–50% DMSO (B)	Ratio B/A
1	Tetraglycine	7.63	9.81	8.32	11.5	1.39
2	Diglycine	8.04	13.7	9.54	15.5	1.62
3	Glycine	9.47	50.0	3.92	154.0	39.3
4	β-Alanine	10.06	89.2	1.91	186.0	97.5
5	γ-Aminobutyric acid	10.41[b]		1.30[c]	232.0	178.5
6	ε-Aminocaproic acid	10.62	203.0	1.21	253.0	209.1
7	L-Alanylglycine	8.07[b]		5.03[c]	6.65	1.32
8	DL-Phenylalanine	9.00	17.6	3.51[c]	49.8	14.2
9	L-Tyrosine	9.00[b]		3.51	66.2	18.8
10	DL-Methionine	9.08	17.6	3.04	66.3	21.8
11	L-Leucine	9.43[b]		2.57[c]	90.0	35.0
12	DL-α-Alanine	9.57	35.3	2.23	81.7	36.6
13	DL-Norleucine	9.63	34.9	2.05	87.0	42.4
14	DL-α-Phenyl-α-alanine	9.12	1.05	0.167	5.35	32.0
15	DL-α-Methylmethionine	9.45	1.56	0.128	6.63	51.8
16	DL-Isovaline	9.98	2.79	0.0715	10.0	140.0
17	α-Aminoisobutyric acid	10.02	3.17	0.0742	13.8	186.1
18	1-Aminocyclopentane-1-carboxylic acid	10.06	4.51	0.0966	17.4	180.1

[a] Values from ref 7 except as indicated. [b] Values from D. D. Perrin "Dissociation Constants of Organic Bases in Aqueous Solutions," Butterworth and Co., Ltd., London 1965. [c] Predicted rate constants calculated by means of eq 5 and 7 in ref 7.

amount of primary amino compound in the reaction mixture and gives negligible color with alkylated amino compounds such as V. The pseudo-first-order kinetic procedure was used to obtain the second-order rate constants k_2 (see Experimental Section).
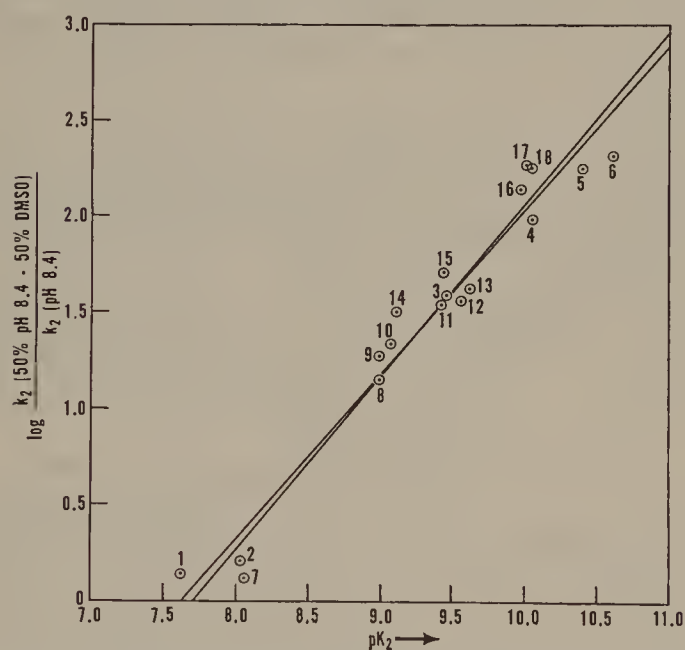
Figure 1. Plot of ratios of second-order rate constants ($k_2 \times 10^4$ in l./mole sec) for the reaction of amino groups in amino acids and peptides with acrylonitrile at 30°. Numbers correspond to compounds listed in Table I.

The standard medium consisted of equal volumes of DMSO and pH 8.4 borate buffer. Rates at pH 8.4 were previously determined at an ionic strength of 1.2, but it was necessary to reduce the ionic strength of the buffer in the mixture to 0.15, because addition of DMSO to buffers of higher ionic strength caused precipitation of KCl. Ionic strength has only a slight effect on reactions of amino and thiol groups with acrylonitrile.[8,9]

Table I summarizes rate data for the reaction of three structurally different series of amino acids and peptides with acrylonitrile. In the first series (1–6), the amino groups are attached to primary carbon atoms; in the second (7–13), to secondary; and in the third (14–18), to tertiary. The amino groups are in a similar steric environment within each series. Second-order rate constants (k_2) in a medium consisting of 50% pH 8.4 buffer–50% DMSO are compared to analogous rate constants determined in the pH 8.4 buffer. The ratio of rates shown in the last column is taken as a measure of the rate-enhancing effect of the added DMSO.

In the pH 8.4 buffer, rates decrease with increasing pK_2 values for each series, because the greater the pK_2 the lower the reactive amino acid anion concentration. Observed rates in the 50% pH 8.4–50% DMSO medium, however, parallel the pK_2 values of the amino groups. Indeed, a plot of the logarithm of the ratio of rates for all 18 compounds against pK_2 values is nearly linear (Figure 1). The straight lines in Figure 1 were drawn by standard least-square fit methods. The required calculations and plotting were performed with an IBM 1130 computer system equipped with an IBM 1627 plotter. The sum of deviations squared in the x direction was taken as a minimum for the steeper line in Figure 1, and the sum of deviations squared in the y direction was taken as a minimum for the other line. The flat line is described by the equation

$$\text{log ratio of rates} = R = 0.855 pK_2 - 6.505 \quad (3)$$

with a standard error of estimate in R of 0.1487. The relationship for R may be used to calculate rate ratios for any amino acid or peptide whose pK_2 is known. For example, the predicted rate ratio for a compound with a pK_2 value of 10 would be 111 ± 14.

The variable rate enhancement of DMSO can be explained in terms of relative participation of H_2O and DMSO in acid–base equilibria and hydrogen-bonding interactions in the ground and transition states.

The pK_2 of an amino acid is a constant that measures not only the concentration of the amino acid anion at any given pH, but also the inherent basicity of an amino group. Observed rates for a sterically similar series

of amino acids and peptides decrease with increasing pK_2 values. The dependence of reaction rates on differences in inherent basicities of amino groups can be deduced by comparing second-order anion rate constants (k_{A^-}) as a function of pK_2 values of amino groups. These rate constants either may be secured directly by carrying out rate studies at a pH about two units above the pK_2 values or may be calculated from rates at any pH by means of the previously derived[7] formula $k_{A^-} = k_2(1 + (H^+)/K_2)$. The anion rate constants which measure maximum rates in aqueous solution are a direct function of the basicities of the amino groups and are pH independent.

Since the observed rate constants in the 50% pH 8.4–50% DMSO medium are also a direct function of the pK_2 values, apparently the added DMSO causes complete ionization of the ammonium group. Some support for this hypothesis comes from the observation that the pH of solutions of all amino compounds in the 50% pH 8.4–50% DMSO medium was between 10.5 and 11.0. Although the validity of such pH readings in mixed aqueous and nonaqueous solvent media could be questioned, all compounds with pK_2 values of 9 or less would be completely ionized in the cited pH range. The effect of DMSO on the ionization equilibrium, however, could not be its only influence for two reasons. First, the observed k_2 values in the mixed medium are greater than the k_{A^-} values by a factor ranging from 1.2 to 5.0 (Table I). This difference signifies that the inherent nucleophilic reactivities of the amino groups are greater in the 50% pH 8.4–50% DMSO solvent medium than the maximum attainable nucleophilicities in aqueous buffers. Second, the slope in Figure 1 (0.855) is double the average slope (0.427) from plots of log k_{A^-} vs. pK_2 values. Rates in the mixed solvent system are more sensitive to changes in pK_2 values than corresponding rates determined in aqueous buffers.

The strong hydrogen-bond donor ability of water will result not only in effective solvation of anions but also in formation of a hydrogen bond with the amino group of the conjugate base of an amino acid, as in A. The

$$
\begin{array}{cc}
\overset{\displaystyle H}{\underset{\displaystyle H}{\overset{|}{\underset{|}{\,^-OOCRN:\cdots H-OH}}}} & \overset{\displaystyle H}{\underset{\displaystyle B}{\overset{|}{\,^-OOCRN-H\cdots\ddot{O}H_2}}} \\
A &
\end{array}
$$
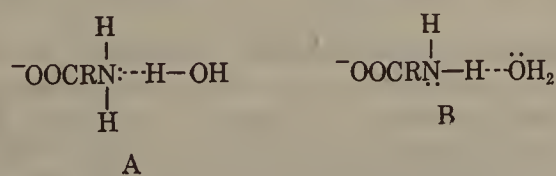
electron density on nitrogen is thereby effectively decreased and, consequently, its nucleophilicity is lowered. This process also counteracts hydrogen-bond donation by the amine to water, as in B, which would enhance nucleophilicity of the nitrogen. In DMSO, only the B-type hydrogen bonding is possible since DMSO is a strong hydrogen-bond acceptor only. The DMSO could therefore increase the nucleophilicity of the conjugate base of an amino acid by (1) decreased solvation of the negative charge in A or B or (2) hydrogen-bond formation between DMSO oxygen and an NH_2 hydro-

$$
\begin{array}{cc}
\overset{}{\underset{\displaystyle H}{\,^-OOCR\ddot{N}-H\cdots\ddot{O}-\overset{+}{S}\overset{CH_3}{\underset{CH_3}{<}}}} & \overset{}{\underset{\displaystyle H \quad H}{\,^-OOCR\ddot{N}-H\cdots\ddot{O}-H\cdots\overset{+}{O}-\overset{+}{S}\overset{CH_3}{\underset{CH_3}{<}}}} \\
C & D
\end{array}
$$
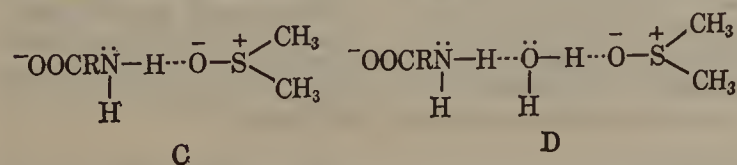
gen, i.e., similar to B or as in C and D. Because of poorer solvation of the negative carboxyl group in the

mixed solvent, C and D ground states would be of higher energy than A and B.

Similar hydrogen-bonding effects may occur in the transition state (eq 2), but because of more diffuse charge and steric bulk, there would likely be less difference in solvation between protic or aqueous solvents and aprotic–dipolar solvents. Since DMSO is more selective in its solvation of the transition state, due to selective solvation of the positive charge, one would expect a more positive ΔS^* for the formation of the transition state in the mixed solvent system than in the aqueous buffer (bulk or steric effect), provided solvation by DMSO does not produce a more ordered system than corresponding solvation by H_2O (ordering or restrictive effect).

Reaction Rates as a Function of pH of the Buffer. The relationship between buffer pH and reaction rates was established by determining the rate constants for reaction of diglycine with acrylonitrile as a function of buffer pH. Table II shows that the rate increases

Table II. Reaction Rate of Diglycine with Acrylonitrile as a Function of pH of the Buffer at 30°

Reaction medium	$k_2 \times 10^3$, l./mole sec	pH[a]
50% H_2O–50% DMSO	0.04	5.5
50% pH 7.5[b]–50% DMSO	0.27	7.6
50% pH 7.9[c]–50% DMSO	1.3	9.3
50% pH 8.4[c]–50% DMSO	1.5	10.6
50% pH 9.0[c]–50% DMSO	1.5	11.8
50% pH 11.0[c]–50% DMSO	1.5	>13.0

[a] Average of measured initial and final pH values of reaction mixture. [b] Tris buffer. [c] Borate buffer.

with pH and becomes constant above pH 8.4. Interestingly, the measured pH values of the reaction media increase in a parallel fashion with the buffer pH.

With a pK_2 value of 8.04, diglycine would be incompletely ionized in a pH 8.4 medium. Since a further increase in pH of the buffer does not result in a corresponding increase in rate in the mixed medium but does cause an increase in rates in the aqueous buffer media, evidently added DMSO favors ionization of the zwitterion to the anion.

Effect of DMSO Concentration on Rates. The effect of varying DMSO concentrations on rates was studied with two peptides and one amino acid (Table III).

Table III. Second-Order Rate Constants ($k_2 \times 10^4$ in l./mole sec) for Reaction of Amino Groups with Acrylonitrile at 30° as a Function of DMSO Concentration

Compd	pH 8.4	20% DMSO	50% DMSO	80% DMSO
Diglycine	9.5	14.4	15.5	2.3
L-Alanylglycine	5.0	6.0	6.3	0.93
α-Aminoisobutyric	0.074	1.32	13.8	21.5

With the peptides, rates pass through a maximum and then decrease with increasing DMSO concentration, whereas with α-aminoisobutyric acid, the rate increases with DMSO concentration. Peptide bonds appear to be responsible for decreased reactivities of the two dipeptides at the higher DMSO concentration, but no

Table IV. Second-Order Rate Constants ($k_2 \times 10^4$ in l./mole sec) for Reaction of Amino Groups with α,β-Unsaturated Compounds at 30°

Compd	k_2,[a] pH 8.4 (A) Diglycine	Glycine	k_2, 50% pH 8.4–50% DMSO (B) Diglycine	Glycine	Ratio B/A Diglycine	Glycine
CH$_2$=CHCONH$_2$	1.3	0.49	0.38	0.41	0.30	0.84
CH$_2$=CHCON(CH$_3$)$_2$	0.21	0.072	0.20	0.29	0.95	4.0
CH$_2$=CHCN	9.5	3.9	15.5	155	1.62	39.3
CH$_2$=CHSO$_2$CH$_3$	62.7		103.0		1.65	

[a] Predicted rates calculated from data in ref 9 by means of eq 1.

obvious explanation can be offered to rationalize this solvent effect.

Reliable data could not be obtained in 100% DMSO medium because of solubility problems.

Effect of Structure of Vinyl Compounds on Rates. Direct evidence which implicates DMSO in hydrogen-bonding interactions comes from a comparison of observed relative reactivities of four vinyl compounds (Table IV). The striking result is that addition of DMSO causes a retardation in the rate with acrylamide. This unexpected behavior must be due to the amide group in acrylamide which may participate in intra- or intermolecular hydrogen bonding with various charged species in the reaction mixture. A possible mechanism for such interactions between the strong dipole of the sulfoxide group in DMSO and the amide group of acrylamide is depicted in E. The indicated hydrogen
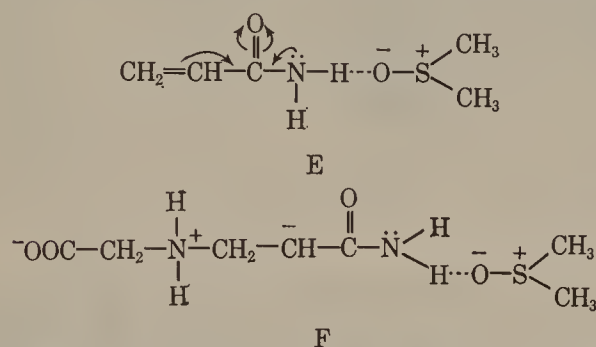
bonding in E would increase the electron density on nitrogen. The resulting greater conjugative interaction (a) of the lone electron pair on nitrogen competes with the conjugative polarization (b) of the π electrons of the carbon–carbon double bond by the carbonyl group. The net effect would be an increased electron density at the terminal carbon atom of acrylamide and a decreased electrophilic reactivity for this vinyl compound. Similar influences operate in the transition state F.

The observed reaction rates for N,N-dimethylacrylamide support this hypothesis. Since the hydrogen-bonding interactions described are not possible, the ratios of reaction rates in the mixed solvent system to those in the aqueous buffer (B/A ratios in Table IV) are three to four times greater for N,N-dimethylacrylamide than the corresponding values for acrylamide.

It should also be pointed out that two additional factors contribute to the electrophilic reactivity of N,N-dimethylacrylamide. These are the steric and inductive influences of the two methyl groups. The electron-donating inductive effect probably enhances the conjugative interaction of the unpaired electrons on nitrogen with the carbonyl group in N,N-dimethylacrylamide. The two parameters are undoubtedly also subject to solvent effects.

Effect of Nonaqueous Solvents on Rates. The effect of varying the nature of the nonaqueous solvents on

Table V. Second-Order Constants ($k_2 \times 10^4$ in l./mole sec) for the Reaction of Amino Groups with Acrylonitrile at 30° as a Function of Nonaqueous Solvent

Reaction medium	Glycine	Diglycine
pH 8.4	3.9	9.5
50% pH 8.4–50% methanol	7.3	8.2
50% pH 8.4–50% acetonitrile	18.0	3.5
50% pH 8.4–50% dimethylformamide	93.0	9.0
50% pH 8.4–50% dimethylacetamide	93.0	7.5
50% pH 8.4–50% dimethyl sulfoxide	155.0	15.5

rates was studied with glycine and diglycine (Table V).

The data in Table V indicate a lack of solvent sensitivity of diglycine as compared to glycine. Interestingly, rates for both glycine and diglycine are similar in the presence of methanol, a nonaqueous protic solvent.

Reactivities of Protein Amino Groups. The progress of reaction of amino groups with acrylonitrile in three proteins at pH 8.4 and in a 50% pH 8.4–50% DMSO medium is illustrated in Figures 2 and 3, respectively. Since amino groups react at different rates in the three proteins and since the expected straight-line pseudo-first-order plots do not generally occur, reactivities change within the same protein. The curvature of the plots is more pronounced in the mixed solvent medium than in the aqueous buffer.

Evidently, readily accessible amino groups on the surface of the protein molecule react at faster rates than analogous amino groups which are partially or fully hidden by folding and helicity of the protein chains.

Furthermore, since inherent basicities of amino groups are a function of their macro- and microscopic environment, acid–base equilibria for amino groups on the same protein chain must also vary. The conformation of the protein and the inherent microscopic and macroscopic basicities of its amino groups in a given reaction medium are probably the dominant factors that govern their nucleophilic reactivities.

Experimental Section

(13) The mention of firm names or trade products does not imply that they are endorsed or recommended by the Department of Agriculture over other firms or similar products not mentioned.
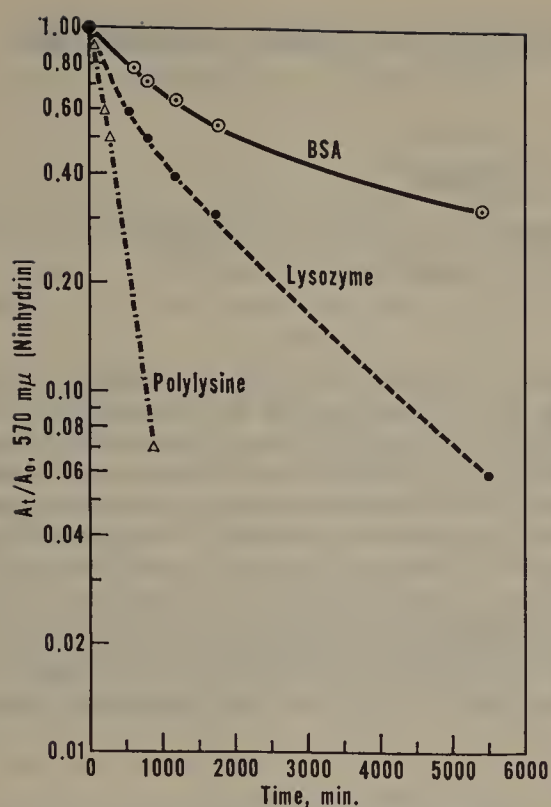
Figure 2. Plot of log A_t/A_0 vs. time for reaction of proteins (0.005 M in NH_2 groups) with acrylonitrile (0.0825 M) in pH 8.4 buffer medium (μ = 0.15) at 30°. BSA stands for bovine serum albumin.
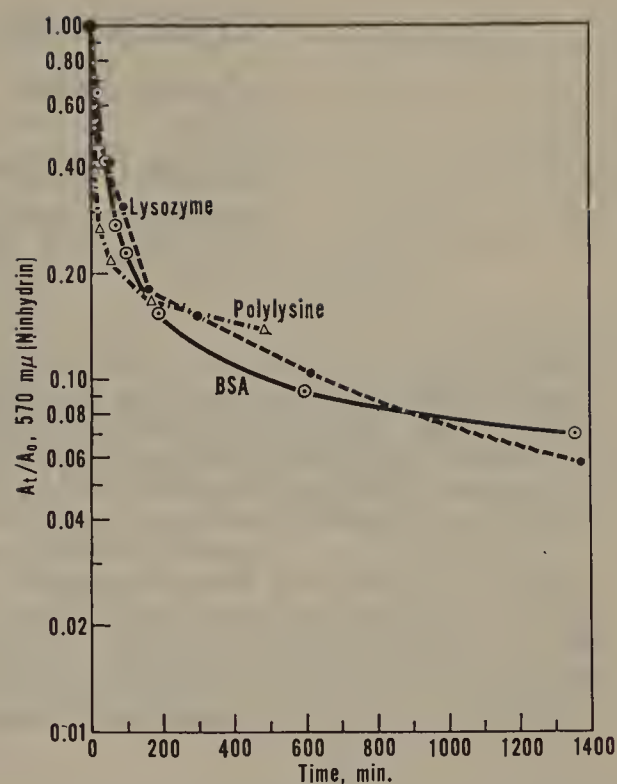
Figure 3. Plot of log A_t/A_0 vs. time for reaction of proteins (0.005 M in NH_2 groups) with acrylonitrile (0.0825 M) in 50% pH 8.4 buffer–50% DMSO at 30°. BSA stands for bovine serum albumin.

Kinetic Measurements. The general procedure has been described.[7] The concentration of the amino compounds ranged between 0.0025 and 0.01 M and that of the vinyl compound in the final mixture was 15 to 20 times in excess over the amino component. Protein concentrations were calculated on the basis of 0.005 M of amino groups. For polylysine, this calculation corresponded to 1.045 g/l. for lysozyme to 12.9 g/l. based on seven amino groups per mole and a molecular weight of 14,200, and for bovine serum albumin to 5.6 g/l., based on 58 amino groups per mole and a molecular weight of 65,000. The final acrylonitrile concentration in the protein solutions was 0.0825 M.

The following is a typical kinetic procedure for the reaction of diglycine with acrylonitrile. The reaction medium was prepared by mixing equal volumes of DMSO and pH 8.4 borate buffer (ionic strength 0.15). The resulting solution was equilibrated in a 30° water bath and used to dissolve 33 mg of diglycine in a 50-ml volumetric flask (solution A). Ten milliliters of this solution was removed by means of a pipet (solution C).

The pH of solution A was 10.6 as read on a TT1C titrator with a titrigraph (Radiometer-Copenhagen). To solution A and to 40 ml of a blank solution consisting of the solvent mixture (solution B) was added 0.15 ml of redistilled acrylonitrile. The tightly stoppered flasks were shaken vigorously and placed in the 30° bath together with one containing solution D, which consisted of the solvent mixture alone. Periodically, 1-ml aliquots were removed

from solutions A, B, C, and D and diluted to 25 ml with water. The ninhydrin color reaction, according to the procedure of Stein and Moore,[14] was carried out in triplicate with three 1-ml aliquots of these dilutions. The fraction of amino components remaining unreacted was calculated from the formula $A_t/A_0 = A_A - (A_B/A_C) - A_D$ = fraction of primary amino compound left in solution A, where A_A, A_B, A_C, and A_D are the absorbances of solutions, A, B, C, and D, and where A_t and A_0 are the corrected absorbances at time t and zero, respectively. The reaction was left running for about four half-lives and the final pH reading of solution A was 10.5.

A plot was made of log A_t/A_0 vs. time. The half-life ($t_{1/2}$) was read from the linear plot, and the pseudo-first-order rate constant (k_1) and second-order rate constant (k_2) were calculated by the formulas $k_1 = 0.693/t_{1/2}$ and $k_2 = k_1$/concentration of vinyl compound.

The precision of the rate determination is illustrated with the following three values for the reaction of diglycine with acrylonitrile in a 50% pH 8.4–50% DMSO medium: $k_2 \times 10^4$ = 1.64, 1.47, and 1.54. Average and standard deviation = 1.55 ± 0.08.

(14) S. Stein and W. H. Moore, *J. Biol. Chem.*, **211**, 907 (1954).

Hydrolytic Mechanisms of Phosphoramidates of Aromatic Amino Acids

Stephen J. Benkovic and Patricia A. Benkovic

Contribution from Department of Chemistry, The Pennsylvania State University, University Park, Pennsylvania 16802. Received May 8, 1967

Abstract: The pH–rate profile for the hydrolysis of o-carboxyphenyl phosphoramidate reveals intramolecular protonated carboxyl group interaction that serves to accelerate the rate of hydrolysis of the monoanionic and neutral species. Hydronium ion catalyzed hydrolysis of o-carboxyphenyl phosphoramidate also is more rapid than the reference compound, p-carboxyphenyl phosphoramidate. Solvolytic experiments in dioxane–water reveal the importance of the zwitterionic form in the hydrolysis of the various phosphoramidate species, in particular the neutral form. Product composition studies in alcohol–water mixtures (methanol, ethanol, 2-propanol, and t-butyl alcohol) reveal: (1) that the product composition in methanol–water (alkyl phosphate:orthophosphoric acid) is independent of the state of ionization of the phosphoramidate; (2) that the product composition is unaffected by the presence of the neighboring carboxyl group; (3) that the phosphorylating species exhibits a marked selectivity for alcohol rather than water; and (4) that steric factors in both substrate and alcohol affect the product composition obtained with the more branched alcohols. These results are discussed in terms of the metaphosphate hypothesis and a bimolecular alternative.

The present investigation was initiated in order to study the possibility of catalyzing intramolecularly the transfer of a phosphoryl moiety to hydroxylic acceptors. Phosphoramidates generally differ from phosphate monoesters in their greater lability at ambient temperatures and thus have been recognized for their potential as biochemical phosphorylating agents[1–6] as well as reagents of synthetic utility.[7–10] To choose one example, an enzyme-catalyzed phosphoryl transfer involving phosphoramidate and hexose has been demonstrated in microsomal preparation from rat liver and kidney.[3] Synthetically the preparation of symmetrical and unsymmetrical esters of pyrophosphoric acid has been achieved with phosphoramidate derivatives.[7–10] It is of interest that attempts to phosphorylate alcohols with monoesters of phosphoramidates (e.g., methyl hydrogen N-cyclohexylphosphoramidate) are generally unsuccessful unless pyridine is present, whereas pyrophosphate formation occurs almost quantitatively in the absence of pyridine.[10] Several quantitative studies have dealt with the hydrolysis of phosphoramidate itself and various N-acyl and N-aryl derivatives.[11,12] Chanley,[11] Jencks,[13] and their co-workers also have shown that the hydrolysis of phosphoramidate monoanion is subject to nucleophilic catalysis by various amines, especially pyridines, and furthermore that the hydrolysis of phosphoramidate is accelerated by electrophilic catalysts including formaldehyde and nitrous and hypochlorous acid. The above studies, however, differed in their conclusions and described the hydrolysis of phosphoramidate monoanion either as strictly bimolecular[11] or in terms of a borderline mechanism not involving a "free metaphosphate" intermediate, the initial product of a unimolecular pathway. Both interpretations were drawn from similar experimental evidence which indicated that the hydrolysis proceeded *via* species that showed a degree of selectivity for nucleophilic reagents. This behavior is not anticipated for a reactive species such as metaphosphate. Moreover, Chanley and Feageson who extended their product composition studies to low pH, thus including the neutral and protonated species of phosphoramidate, encountered a change in product composition. This result was interpreted on the basis of a change to a metaphosphate mechanism. It therefore became important to investigate what effect intramolecular catalysis, the state of ionization of the phosphoramidate, and the nature of the nucleophile might have on product composition, and ultimately to attempt a formulation of a general mechanism for phosphoramidate hydrolysis.

Experimental Section

All melting points are uncorrected. Microanalyses were performed by Midwest Microlabs. Infrared spectra were obtained with a Perkin-Elmer 237B spectrophotometer. Kinetic solutions were prepared from freshly boiled distilled water tested for inorganic ions with EDTA. In alcohol–water experiments all alcohols were either reagent or spectrophotometric grade (Fisher). Reagent grade salts and acids (Fisher, Baker) were used without further purification. Dioxane was purified by the method of Fieser,[14] stored over sodium, and distilled prior to use.

Materials. Dicyclohexylammonium o-Carboxyphenyl Phosphoramidate. Synthesis of the phosphoramidic dichloride precursor, (o-ClCOC₆H₄NHPOCl₂), was by the method of Uhlfelder,[15] mp 62° (lit.[15a] mp 62°); infrared absorption (Nujol) at

(1) A. Fujimoto and R. A. Smith, *Biochim. Biophys. Acta*, **56**, 501 (1962).

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(9) J. G. Moffatt and H. G. Khorana, *ibid.*, **80**, 3756 (1958).

(10) N. K. Hamer, *J. Chem. Soc.*, 46 (1965).

(11) J. D. Chanley and E. Feageson, *J. Am. Chem. Soc.*, **85**, 1181 (1963); **80**, 2686 (1958).

(12) M. Halmann, A. Lapidot, and D. Samuel, *J. Chem. Soc.*, 3158 (1961), and references therein.

(13) W. P. Jencks and M. Gilchrist, *J. Am. Chem. Soc.*, **86**, 1410 (1964); **87**, 3199 (1965).

(14) L. F. Fieser, "Experiments in Organic Chemistry," D. C. Heath and Co., Boston, Mass., 1957, p 284.

(15) (a) E. Uhlfelder, *Chem. Ber.*, **36**, 1824 (1903). (b) The structures of the precursors merit further investigation, especially in view of the elucidation of the structure of Couper's compound [A. G. Pinkus,

3.14, 5.68, 5.85, 622, 6.33, 7.73 (doublet), 8.34, 10.5, 11.4, 13.1, and 13.5 μ. The phosphoramide dichloride (1.9 g, 7.0 × 10⁻³ mole) was added over a 15-min period to a vigorously stirred ice-cold slurry of Ag₂CO₃ (3.4 g, 1.2 × 10⁻² mole) in 30 ml of 50% v/v acetone–water. The mixture was filtered and the precipitate washed with 10 ml of water. To the combined filtrate and washings (maintained ice cold), cyclohexylamine was added dropwise until the initially formed precipitate disappeared (ca. pH 8).[16] The resultant clear solution was diluted with acetone until turbid, then chilled for 1 hr in ice. Filtration of the white, crystalline salt gave 0.65 g (1.6 × 10⁻³ mole) of dicyclohexylammonium *o*-carboxyphenyl phosphor-amidate, mp 135–137°. The compound was stored at 0° in the dark. No attempts were made to maximize the yield; infrared absorption (Nujol) at 3.00 (broad), 3.20, 3.80 (broad), 6.20, 6.32 (broad), 7.83 (broad), 8.70, 9.30 (broad), 10.6 11.1, and 13.3 μ. Recrystallization was achieved from acetone–water solutions.

Anal. Calcd for $C_{19}H_{34}N_3O_5P \cdot 0.5H_2O$: C, 53.76; H, 8.31; N, 9.90; P, 7.30. Found: C, 53.94; H, 8.54; N, 10.02; P, 6.30; P, 7.12 (method of Martin and Doty, see below).

Tricyclohexylammonium *p*-Carboxyphenyl Phosphoramidate. Synthesis of the phosphoramidic dichloride precursor (*p*-ClCO-$C_6H_4NHPOCl_2$) was by the method of Michaelis,[17a] mp 156–157°,[17b] softening and resolidification noted at 134–135° (lit.[17a] mp 168°); infrared absorption (Nujol) at 3.19, 5.66, 5.76, 6.24, 6.62, 7.70, 8.11 (multiplet), 8.60, 10.5, 11.3, 11.8, 12.7, and 13.9 μ. The phosphoramidic dichloride[18] (2.0 g, 7.3 × 10⁻³ mole) was added over a 15-min period to a vigorously stirred, ice-cold slurry of Ag₂CO₃ (3.5 g, 1.2 × 10⁻² mole) in 30 ml of 83% v/v acetone–water. The mixture was filtered and the precipitate washed with 10 ml of water. The combined filtrate and washings (maintained ice cold) were then treated with Norit and filtered, and the clear solution was brought to ca. pH 10 by rapid dropwise addition of cyclohexylamine. The resultant clear solution was diluted with acetone until turbid, then chilled in ice overnight. Collection of the white crystalline salt gave 0.57 g (1.1 × 10⁻³ mole) of tricyclohexyl-ammonium *p*-carboxyphenyl phosphoramidate, mp 153–155°. The compound was stored at 0° in the dark; infrared absorption (Nujol) at 2.98 (broad), 3.14, 3.80 (broad), 6.12, 6.20, 6.35 (broad), 7.63, 8.76, 9.45 (broad), 10.3, 11.1, 12.7, and 13.9 μ.

Anal. Calcd for $C_{25}H_{48}N_4O_5P \cdot 2H_2O$: C, 54.42; H, 9.13; N, 10.15; P, 5.61. Found: C, 54.68; H, 9.28; N, 10.44; P, 4.64; 5.73 (method of Martin and Doty).

Apparatus. Instrumentation used in this study has previously been described.[20] Kinetic runs of greater than 12-hr duration and product composition studies were carried out in Kimax (No. 45066) screw-cap tubes maintained at reaction temperature (±0.1°) by immersion in a circulating water bath. Shorter runs were conducted in thermostated, 2-cm stoppered cuvettes.

Kinetics. The hydrolysis of *o*-carboxyphenyl phosphoramidate was monitored at 245 mμ following the decrease in absorption due to fission of the P–N bond or by analysis for orthophosphate by the method of Martin and Doty[21] as modified by Jencks.[13] Reactions (spectrophotometric) were initiated by the addition of *o*-carboxyphenyl phosphoramidate (ca. 1 mg) by means of a micro-spatula directly into the preequilibrated buffer solution (pH >0.5, μ = 0.2, KCl). The cuvette was inverted and allowed to reequili-brate for 5 min before absorbance readings were taken. Reactions (orthophosphate analysis) were initiated by the addition of *o*-carboxyphenyl phosphoramidate (3–4 mg) to 10 ml of the pre-equilibrated buffer solutions, and 1-ml aliquots were withdrawn at the desired time intervals. Buffers employed were hydrochloric acid

(pH <2.5),[22] formate (0.2 *M*, pH 3.0–3.8), acetate (0.2 *M*, pH 4.0–5.4), succinate (0.067 *M*, pH 5.7–6.1), imidazole (0.01 *M*, pH 6.7–7.0), and Tris (0.2 *M*, pH 7.6–8.1). No acceleratory buffer effects were noted although higher concentrations of imidazole (up to 0.2 *M*) had a slight retarding effect on the observed rate. The pH of the kinetic runs was measured at 35° (glass electrode) upon initiation and after completion of the runs; those exhibiting pH drift greater than ±0.02 unit were discarded. The rate of hy-drolysis of the *p*-carboxyphenyl phosphoramidate was followed by analysis for the liberated orthophosphate.

The observed first-order rate constants (spectrophotometric or phosphate analysis)[23] for hydrolysis of *o*-carboxyphenyl phos-phoramidate were calculated from slopes of plots of log [(OD∞ − OD₀)/(OD∞ − OD$_t$)] or log [OD∞ − OD$_t$] against time. Plots were generally linear to at least three half-lives. Rate constants determined by the two methods agreed within ±3%. Duplicate runs by a given method agreed within ±3%. No buffer effects (formate, 0.06–0.2 *M*, pH 3.08) were noted, Kinetic runs at pH <0.5 were carried out at μ = 1.0, KCl; those in 1.0–3.0 *N* HCl at μ = 3.0, KCl.

The observed first-order rate contants for hydrolysis of *p*-carboxyphenyl phosphoramidate were measured by phosphate analysis and calculated as discussed above. No buffer effects (formate, 0.1–0.2 *M*, pH 3.08) were noted. Kinetic runs at pH <0.5 were carried out at μ = 1.0, KCl.

Kinetic runs for solvolysis of *o*-carboxyphenyl phosphoramidate conducted in mixed solvents (methanol–water, dioxane–water) were followed spectrophotometrically. The compositions of the solvent mixtures were obtained by mixing measured volumes of the nonaqueous and aqueous components. The desired pH was maintained by the above buffers; all solutions were at μ = 0.2, KCl.

The ionization constants of *o*- and *p*-carboxyphenyl phosphor-amidate were determined by the method of half-neutralization in both aqueous and mixed solvents. The accuracy of these measure-ments is impaired by the lability of these compounds; reported pK_a's have an estimated error of ±0.2 pK_a unit (Table I).

Table I. Dissociation Constants of *o*- and *p*-Carboxyphenyl Phosphoramidates (μ = 0.2, 35°)

Solvent	o-Carboxy			p-Carboxy		
	pK_1^a	pK_2	pK_3	pK_1^a	pK_2	pK_3
H₂O	2.17	4.43	7.25	2.63 (2.37)[b]	5.14 (5.04)[b]	6.99
53% v/v CH₃OH–H₂O[c]	3.06	…	8.14	2.86	…	7.72

[a] No hydrogen ion correction applied. [b] Duplicate values, values not in parentheses used in actual calculation of rate con-stants. [c] pH measurements are uncorrected for solvent effects on the glass electrode.

Products. Spectrophotometric scanning (240–340 mμ) at t_∞ of *o*- and *p*-carboxyphenyl phosphoramidate kinetic solutions of known concentration disclosed an ultraviolet spectra identical with quantitative liberation of anthranilic and *p*-aminobenzoic acids, re-pectively. Exclusive P–N bond cleavage is the general mode of bond fission for phosphoramidates.[24] The absence of detectable reaction intermediates in the hydrolysis of *o*-carboxyphenyl phos-phoramidate at significant concentrations is implied by the lack of any observable lag phase in the kinetics and the identical rate con-stants as measured by substrate disappearance and product ap-pearance. Paper chromatography of the hydrolysis products of *o*-carboxyphenyl phosphoramidate by the method of Karl Kroupa[25] utilizing pyrophosphate and orthophosphate as reference stand-ards revealed only orthophosphate, no pyrophosphate being de-tected.

In alcohol–water solvents the mole fraction of orthophosphate was calculated from the ratio of orthophosphate concentrations

P. G. Waldrep, and S. Y. Ma, *J. Heterocyclic Chem.*, **2**, 357 (1965)]. The analytic, infrared, and kinetic data, however, indicate that the desired phosphoramidates are formed upon partial hydrolysis.

(16) Isolation of the initial precipitate, presumably the monocyclo-hexylammonium salt, yielded a compound which rapidly decomposed upon drying over CaCl₂ at room temperature.

(17) (a) A. Michaelis, *Ann.*, **326**, 129 (1903). (b) The compound appears to fuse upon heating and an accurate melting point is difficult to determine.

(18) The synthesis of the above phosphoramidic dichlorides is accom-plished under differing reaction conditions (solvent, temperature) than utilized in the synthesis of phosphoazoaryls from arylamines and PCl₅.[19] Furthermore, POCl₃ is generated in the above reactions. See, how-ever, 15b.

(19) I. Zhmurova and A. V. Kirsanov, *Zh. Obshch. Khim.*, **30**, 3044, 4048 (1960).

(20) S. J. Benkovic and P. A. Benkovic, *J. Am. Chem. Soc.*, **88**, 5504 (1966).

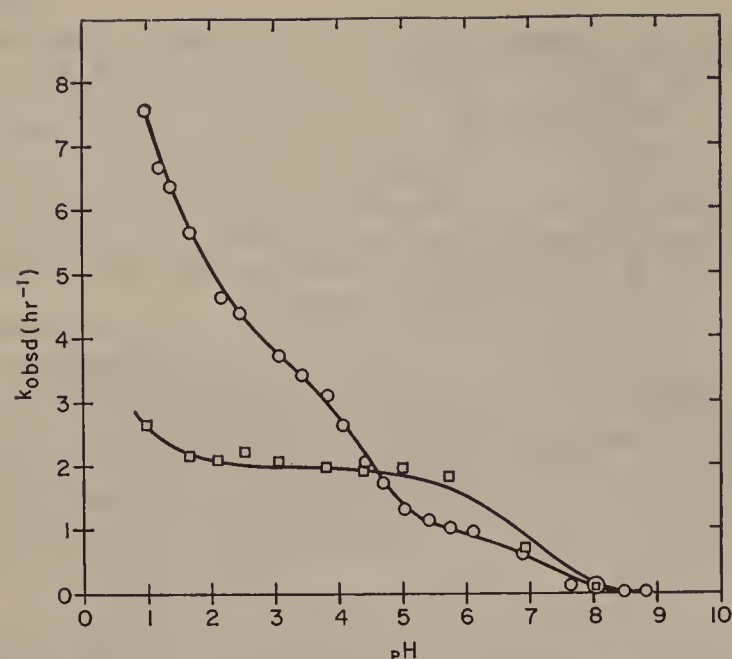(21) J. B. Martin and D. M. Doty, *Anal. Chem.*, **21**, 965 (1949).

(22) No correction was applied for the small error incurred in reading pH values between pH 0 and 1.

(23) Development procedure for analysis of orthophosphate resulted in less than 5% hydrolysis of the phosphoramidate substrate.

(24) T. C. Bruice and S. J. Benkovic, "Bioorganic Mechanisms," Vol. II, W. A. Benjamin, Inc., New York, N. Y., 1966, Chapter 5.

(25) E. Karl-Kroupa, *Anal. Chem.*, **28**, 1091 (1956).

Figure 1. The pH–rate profiles for the hydrolysis of o-carboxy-phenyl phosphoramidate, O, and p-carboxyphenyl phosphorami-date, □, at 35°, $\mu = 0.2$. Solid line is theoretical curve calculated from values listed in Table II.

measured at t_∞ in these solvents to the known value of orthophosphate concentration at t_∞ in aqueous solution. In practice this was accomplished by measuring the OD at t_∞ of aliquots of the alcohol–water mixture containing known concentrations of the phosphoramidates by the development procedure of Martin and Doty. Additional aliquots were withdrawn at ca. 1–2-hr intervals until successive readings agreed within experimental error. The method of Martin and Doty is specific for orthophosphate; phosphate monoesters are not hydrolyzed by the development conditions. The OD_∞ for hydrolysis of an identical concentration of phosphoramidate in aqueous solution was determined from standard curves of optical density vs. concentration. The ratio of the above OD_∞ (alcohol–water : water) is, therefore, the mole fraction of orthophosphate as the solvolysis product. At the temperature and pH's employed the solvolyses of the phosphoramidates are much faster than either of the possible competing reactions, solvolysis of products or esterification of phosphoric acid.[26] The mole fraction alkyl phosphate formed in each solvent mixture was calculated from 1.0 − mole fraction of orthophosphate.

Paper chromatography by the method of Chanley and Feageson[11] of the solvolyses of o-carboxyphenyl phosphoramidate in methanol–water utilizing orthophosphate, pyrophosphate, and methyl phosphate as reference standards revealed methyl phosphate and orthophosphate as the solvolytic products. The pH of the chromatographed solutions was 2.28, 3.76, and 6.25.

The presence of isopropyl phosphate in the solvolysis of p-carboxyphenyl phosphoramidate in 30% v/v 2-propanol–water was demonstrated by (1) the development procedure described above and (2) acidification of aliquots of the solvolysis solution to pH 0.3 and incubation at 75° for 8 days at which time the development procedure indicated ca. 50% of an acid-hydrolyzable phosphate had disappeared. Paper chromatography revealed no pyrophosphate in the original solvolytic media at t_∞.

Results

Kinetics. The pH–rate profiles for the hydrolysis of o-carboxyphenyl phosphoramidate (1) and p-carboxyphenyl phosphoramidate (2) are exhibited in Figure 1. Pertinent kinetic data are summarized in Table II. A generalized kinetic equation applicable to both 1 and 2 may be developed by assuming all species to be subject to hydrolysis excluding the phosphoramidate trianion (experimentally shown as relatively stable). The following dissociation constants may be defined and identified with those measured experimentally.[27]

(26) By comparison to the data of ref 11.

(27) K_1, K_2, and K_3 because of the multiple protonation sites are

$$K_1 = \frac{[a_H][\text{HOOC--R--NHPO}_3\text{H}^-]}{[\text{HOOC--R--NHPO}_3\text{H}_2]}$$

$$K_2 = \frac{[a_H][^-\text{OOC--R--NHPO}_3\text{H}^-]}{[\text{HOOC--R--NHPO}_3\text{H}^-]}$$

$$K_3 = \frac{[a_H][^-\text{OOC--R--NHPO}_3{}^{2-}]}{[^-\text{OOC--R--NHPO}_3\text{H}^-]} \quad (1)$$

The over-all rate of hydrolysis at any pH is given by

$$v = k_{H^+}[a_H][\text{HOOC--R--NHPO}_3\text{H}_2] +$$
$$k_1[\text{HOOC--R--NHPO}_3\text{H}_2] +$$
$$k_2[\text{HOOC--R--NHPO}_3\text{H}^-] +$$
$$k_3[^-\text{OOC--R--NHPO}_3\text{H}^-] \quad (2)$$

where k_{H^+} is the second-order rate constant associated with hydronium ion catalyzed hydrolysis of the neutral species; k_1, k_2, and k_3 are defined as first-order rate constants for hydrolysis of the neutral, mono- and dianionic species, respectively. Inclusion of a hydronium

Table II. Rate Constants for the Hydrolysis of o- and p-Carboxyphenyl Phosphoramidates (35°, $\mu = 0.2$)

Compd	k_{H^+}, M^{-1} hr^{-1}	k_1,[a] hr^{-1}	k_2,[a] hr^{-1}	k_3,[a] hr^{-1}
o-COOH	17.6	6.00 (10.0)[b] (7.5)[c]	3.55	0.90
p-COOH	5.4	2.10	1.99	1.63
p-Cl[d]	0.88	0.23		0.034[f]
NH₂PO₃H₂[e]	33.3	0.420		0.252[f]

[a] May also be expressed as second-order rate constants by dividing by 55.5. [b] Extrapolated intercept value of k_{obsd} vs. (0–3.0 M) HCl, $\mu = 3.0$. [c] Extrapolated intercept value of k_{obsd} vs. (0–1.0 M) HCl, $\mu = 1.0$. [d] From the data of Chanley and Feageson[11] (0°, $\mu = 2.0$). [e] From the data of Chanley and Feageson[11] (36.8°, $\mu = 0.2$). [f] Monoanion species.

ion term is justified by the general observation of such catalysis in the hydrolysis of phosphoramidates,[24] except in N-acylphosphoramidates where the acyl group is strongly electron withdrawing. No assumptions have been made, at this point, as to the order of solvent participation in the hydrolysis of any species. Since

$$v = k_{obsd}[\text{phosphoramidate}]_T \quad (3)$$

where

$$[\text{phosphoramidate}]_T = \sum[\text{species}]$$

substitution of the relationships of eq 1 into 2 and 3 then gives

$$k_{obsd} = \frac{a_H{}^2(k_{H^+}a_H + k_1) + K_1(k_3 K_2 + k_2 a_H)}{K_1 K_2[1 + K_3/a_H] + a_H[K_1 + a_H]} \quad (4)$$

The values of k_{obsd} calculated from eq 4 utilizing the rate constants listed in Table II and the experimentally determined dissociation constants are in satisfactory agreement with the experimental points for both 1 and 2.

The pH–rate profile of 1 indicates that successive protonation of the substrate results in an increase in

macroscopic dissociation constants. Consequently the actual and/or hydrolytically important species may not be those bracketed. This is, of course, also true for the kinetic expression 2; later, the various kinetically indistinguishable cases will be examined.
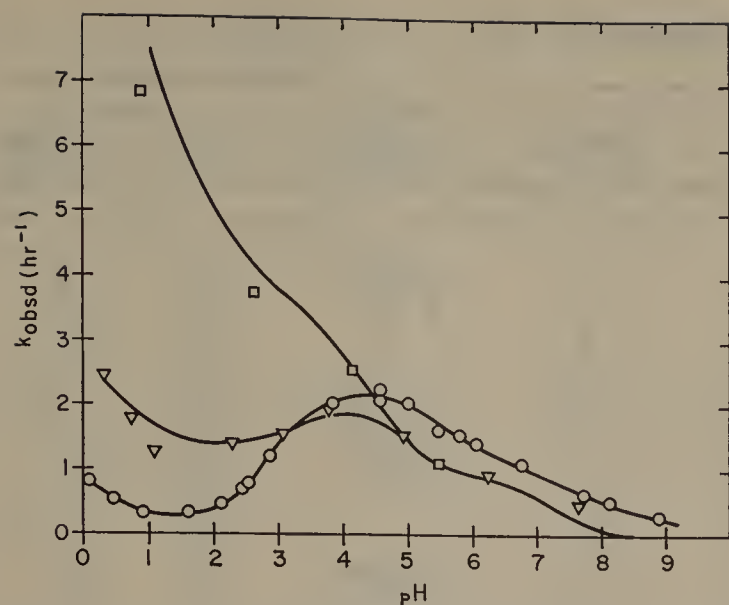
Figure 2. The pH–rate profiles for the solvolysis of *o*-carboxy-phenyl phosphoramidate in 50% v/v dioxane–water, O; 53% v/v methanol–water, △; and 5% v/v methanol–water, □, at 35°, $\mu = 0.2$. Values of k_{obsd} determined in 5% v/v methanol–water are plotted in relation to the pH–rate profile described in Figure 1.

k_{obsd}. The order of rate constants is $k_{H^+} > k_1 > k_2 > k_3$. This contrasts with the pH–rate profile of **2** which exhibits a broad pH-independent region (pH 1.5–6) and rate constants in the order $k_{H^+} > k_1 \approx k_2 \approx k_3$.

Solvolysis of **1** in mixed solvents, 50% dioxane–water and 53% methanol–water, results in a dramatic change both in the magnitude and pH dependency of k_{obsd} (Figure 2). Only at pH >5 does any semblance remain to the original pH–rate profile. Allowing for the shift of pK's to higher values in both mixed solvents (see also ref 11) it appears that only k_3 is essentially unperturbed. The rapid hydrolysis of the neutral and the monoanionic species is severely repressed in both solvents. Participation by the *o*-carboxyl group is no longer manifested by the appearance of a titration curve between pH 3 and 5.

Marked repression of hydrolysis of the neutral species by dioxane–water mixtures has been observed by Chanley and Feageson in the solvolysis of *p*-chloro-phenyl phosphoramidate. In contrast the solvolysis of phosphoramidate itself is accelerated at all pH's in 50% methanol–water relative to purely aqueous media. In the present case the solvolysis of **1** in 5% methanol–water describes a pH–rate profile that closely approximates that observed in purely aqueous solution.

Products. Results of solvolysis experiments on **1** and **2** in alcohol–water mixtures are listed in Table III. Findings for methanol–water mixtures are presented graphically in Figures 3 and 4. The important features of these plots are that (1) the mole fraction of methyl phosphate produced is greater than the mole fraction of methanol in the solvent mixture and (2) the mole fraction of methyl phosphate produced is independent of pH. This is true for both **1** and **2**. This behavior is not readily rationalized at all pH values in terms of a simple bimolecular rate expression where

mole fraction of $CH_3OPO_3H_2 =$

$$\frac{k_{CH_3OH}[CH_3OH]}{k_{CH_3OH}[CH_3OH] + k_{H_2O}[H_2O]} \quad (5)$$

because of the decrease in k_{obsd} in 53% methanol–water
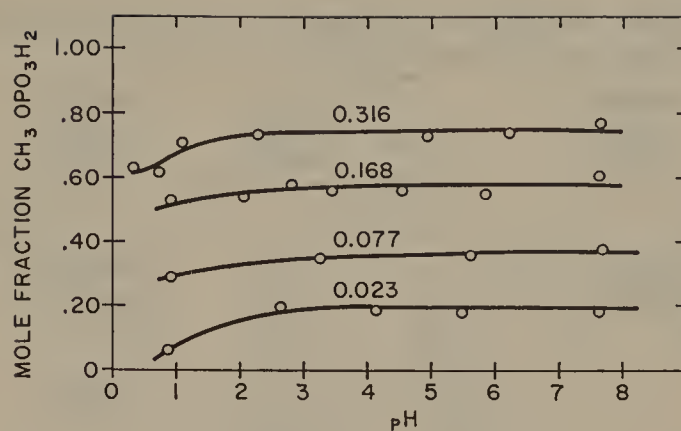
Figure 3. Plots of the mole fraction $CH_3OPO_3H_2$ *vs.* pH for solvolysis of *o*-carboxyphenyl phosphoramidate ($\mu = 0.2$, 35°). Values above the curves are the mole fraction of methanol in the methanol–water solvent.
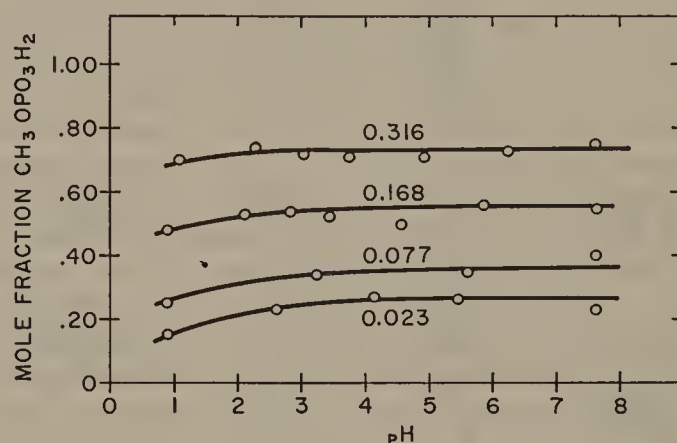
Figure 4. Plots of the mole fraction $CH_3OPO_3H_2$ *vs.* pH for solvolysis of *p*-carboxyphenyl phosphoramidate ($\mu = 0.2$, 35°). Values above the curves are the mole fraction of methanol in the methanol–water solvent.

relative to purely aqueous media which exceeds at pH <3 the decrease in the concentration of water.

With more substituted alcohols, ethanol, 2-propanol, and *t*-butyl alcohol the mole fraction of alkyl phosphate produced decreases but generally exceeds the mole fraction of alcohol in the solvent. This decrease is also somewhat sensitive to the nature of the phosphor-amidate; **1** yields less alkyl phosphate than **2**. With *t*-butyl alcohol, alkyl phosphate is only detected with **2**.

Discussion

It is convenient to analyze the results in terms of each ionic species.

Anions [$^-OOC–R–NHPO_3H^-$] and [HOOC–R–NH-PO_3H^-$]. Phosphate monoester monoanions have been postulated to undergo hydrolysis *via* a unique mechanism generating monomeric metaphosphate.[24,28–30] Evidence has been reported recently that suggests that this pathway probably involves a zwitterionic intermediate.[29]

$$PO_3^- + H_2O \xrightarrow{fast} H_2PO_4^-$$
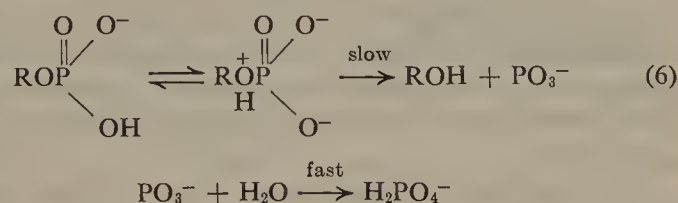
(28) J. R. Cox and O. B. Ramsay, *Chem. Rev.*, **64**, 317 (1964), and references therein.
(29) A. J. Kirby and A. G. Varvoglis, *J. Am. Chem. Soc.*, **89**, 415 (1967).
(30) W. P. Jencks, *Brookhaven Symp. Biol.*, **15**, 134 (1962).

Table III. Variation of Mole Fraction of Alkyl Phosphate with pH upon Solvolysis of o- and p-Carboxyphenyl Phosphoramides ($35°$, $\mu = 0.2$)

Alcohol (mole fraction)	pH	Mole fraction	Alcohol (mole fraction)	pH	Mole fraction	Alcohol (mole fraction)	pH	Mole fraction
ortho								
CH_3OH (0.316)	0.34[a]	0.63	CH_3OH (0.077)	0.92	0.29	C_2H_5OH (0.016)	0.95	0[b]
	0.74[a]	0.62		3.25	0.35		2.58	0[b]
	1.10	0.71		5.61	0.36		4.18	0[b]
	2.28	0.75		7.64	0.38		5.52	0[b]
	3.06	0.73	CH_3OH (0.023)	0.87	0.06		7.64	0.16
	3.74	0.72		2.62	0.20	C_3H_7OH (0.094)	0.98	0[b]
	4.95	0.73		4.14	0.19		2.88	0[b]
	6.23	0.74		5.47	0.18		4.61	0.15
	7.65	0.77		7.63	0.18		5.96	0.14
CH_3OH (0.168)	0.91	0.53	C_2H_5OH (0.116)	1.00	0.27		7.56	0.22
	2.06	0.54		2.84	0.27	C_4H_9OH (0.098)	1.00	0[b]
	2.83	0.58		4.61	0.22		4.61	0[b]
	3.45	0.56		5.95	0.18			
	4.55	0.55		7.59	0.35			
	5.86	0.55						
	7.64	0.61						
para								
CH_3OH (0.316)	1.09	0.70	C_2H_5OH (0.116)	0.99	0.25	C_4H_9OH (0.098)	0.98	0.21
	2.28	0.74		2.85	0.31		5.95	0.19
	3.04	0.72		4.60	0.28			
	3.76	0.71		5.94	0.35			
	4.95	0.71		7.59	0.35			
	6.25	0.73	C_2H_5OH (0.016)	0.95	0[b]			
	7.65	0.75		2.59	0.11			
CH_3OH (0.168)	0.90	0.48		4.18	0.10			
	2.10	0.53		5.52	0.10			
	2.83	0.54		7.64	0.16			
	3.45	0.52	C_3H_7OH (0.094)	0.98	0.15			
	4.56	0.50		2.88	0.16			
	5.86	0.56		4.61	0.20			
	7.64	0.55		5.96	0.15			
CH_3OH (0.077)	0.88	0.25		7.56	0.18			
	3.25	0.34						
	5.61	0.35						
	7.63	0.40						
CH_3OH (0.023)	0.88	0.15						
	2.62	0.23						
	4.14	0.27						
	5.47	0.26						
	7.63	0.23						

[a] $\mu = 1.0$. [b] Zero within experimental error $\pm 4\%$.

It is possible that zwitterion formation may become partially rate determining depending on the nature of the RO group. Solvolysis of phosphate monoanion species in alcohol–water mixtures generally gives rise to a product distribution that closely approximates the mole fraction solvent composition.[11,29] Such a reactive species as metaphosphate is anticipated to be insensitive to the relative nucleophilicity of the various solvent components. This, in a strict sense, is only true for a solvent mixture where both nucleophiles are sterically similar (methanol–water), and it is not expected to be valid in a solvent mixture such as 2-propanol– or t-butyl alcohol–water mixtures. The methanol–water results, along with much other experimental evidence,[24,28,30] have been cited in support of the intermediacy of meta-phosphate.

The hydrolysis of phosphoramidates is more complex. The monoanion of phosphoramidate exists as the zwitterion in the crystalline state.[31,32] a fact revealed by X-ray crystallographic studies. It is also probably zwitterionic in aqueous solution since the second dissociation constant of phosphoramidate ($pK_2 = 8.2$) is significantly smaller than the reference compounds, N-benzoylphosphoramidate ($pK_2 = 5.67, 6.42$) and ethyl N,N-diethylphosphoramidate ($pK_2 = 7.2$).[11,33–35] In contrast the N-aryl derivatives, e.g., p-chlorophenyl phosphoramidate ($pK_2 = 6.8$) and compounds **1** ($pK_3 = 7.25$) and **2** ($pK_3 = 6.99$), have second dissociation constants that appear to be normal; thus the non-zwitterionic form is probably the extant species. One may arrive at the same conclusion qualitatively by considering the phosphoramidate as a bimolecular species comprised of orthophosphoric acid and the corresponding amine. In the case of the aromatic amines $pK_a <$ pK_2 (7.2) of orthophosphoric acid; hence the thermodynamically favored site of protonation is one of the phosphoryl oxygens. In the case of the aliphatic amines

(31) E. Hobbs, D. E. C. Corbridge, and B. Raistrick, *Acta Cryst.*, **6** 621 (1953).
(32) D. E. C. Corbridge and E. J. Lowe, *J. Chem. Soc.*, 493 (1954).

(33) C. Zioudrou, *Tetrahedron*, **18**, 197 (1962).
(34) M. Halmann, A. Lapidot, and D. Samuel, *J. Chem. Soc.*, 4672 (1960).
(35) E. W. Crunden and R. F. Hudson, *ibid.*, 3591 (1962).

$pK_a > pK_2$ of orthophosphoric acid; thus zwitterion formation is anticipated.

Comparison of k_2 and k_3 for **1** and **2** shows that $k_3(\mathbf{2}) > k_3(\mathbf{1})$ whereas $k_2(\mathbf{1}) > k_3(\mathbf{1})$ and $k_2(\mathbf{2})$. It appears that carboxyl group participation may be important in $k_2(\mathbf{1})$ and may be occurring through one of several possible mechanisms.

$$\text{(structure)} \xrightarrow{via\,PO_3^-} \text{products} \quad (7a)$$
$$\xrightarrow{H_2O} \quad (7b)$$

$$\text{(structure)} \xrightarrow{intramolecular} \text{products} \quad (7c)$$
$$\xrightarrow{H_2O} \quad (7d)$$
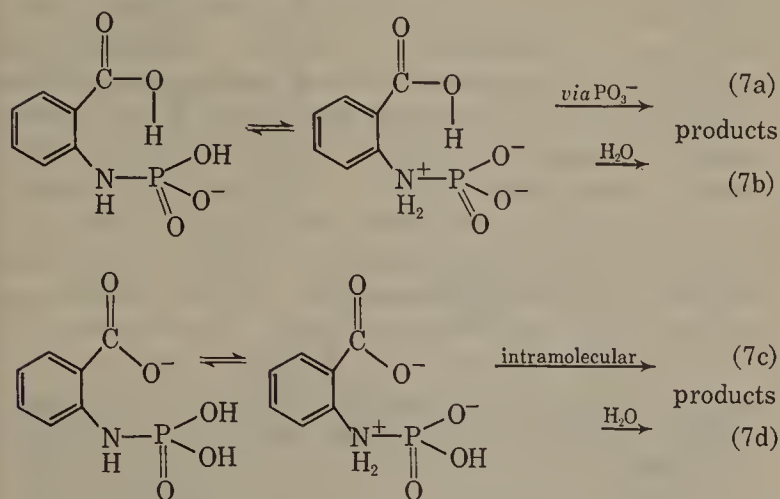
The available experimental evidence does not allow one to distinguish between the above and other possibilities which include: (1) formation of metaphosphate (7a) possibly assisted by intramolecular proton transfer which would be subsequent or concurrent to P–N bond fission; (2) bimolecular pathways b and d involving water as a participating nucleophile with the possibility of proton transfer or electrostatic stabilization respectively; (3) intramolecular phosphoryl transfer (7c) to yield an acyl phosphate[36] which then undergoes hydrolysis. Not shown are possible mechanisms featuring hydronium ion as the proton donor or intramolecular general base catalysis by the carboxylate anion. It seems reasonable on chemical grounds to assume that a zwitterionic species is that subject to hydrolysis. Pathway 7a is similar to but not identical with those postulated in salicyl phosphate[37] and sulfate[38] hydrolysis, which appear to involve a preequilibrium proton transfer, and analogous to the prior observed electrophilic-catalyzed hydrolysis of phosphoramidate itself. A related example of carboxyl group facilitation of hydrolysis may be present in N-phosphorylcreatine.[5] The acceleration due to the neighboring carboxyl group is much less in the present system than in salicyl phosphate where a factor of roughly 10^2 is observed and may be restricted simply to some form of electrostatic interaction, the effects of which are usually less pronounced.[24] It is difficult to rationalize $k_3(\mathbf{1}) < k_3(\mathbf{2})$, since attractive pathways are available for the hydrolysis of this species. No unequivocal explanation can be offered at this time.

Additional mechanistic information may be gained from rate studies in mixed solvents (53% methanol–water, 50% dioxane–water) that indicate $k_3(\mathbf{1})$ is effectively unperturbed while k_2 is depressed (*ca.* 30%). It is known that zwitterion equilibrium is solvent sensitive,

$$\text{(structure)} \xrightarrow{via\,PO_3^-} \text{products} \quad (8a)$$
$$\xrightarrow{H_2O} \quad (8b)$$

decreasing approximately linearly with increasing alcohol and dioxane molarity in the solvent mixture.[39] From considerations discussed above, the mono- and dianions should predominantly exist as the nonzwitterionic species. Insofar as it is applicable, *p*-aminobenzoic and anthranilic acids are effectively nonzwitterionic in aqueous solution.[39] Furthermore it is thought that the hydrolysis of phosphoramidate and *p*-chlorophenyl phosphoramidate monoanions apparently does not involve proton transfers in the rate-determining step due to the absence of substantial deuterium solvent isotope effects.[11] Thus one anticipates that k_{obsd} is directly proportional to K_{zw} where K_{zw} is defined as an equilibrium constant between nonzwitterionic and zwitterionic forms.[40] If one accepts this hypothesis it becomes necessary to postulate that the reaction of the $[^-OOC–RNH_2^+–PO_3^{2-}]$ species is kinetically accelerated by solvents of decreasing polarity to compensate for the decrease in K_{zw}. Assuming the hydrolysis involves a transition state with charge dispersal or neutralization relative to the ground state, then the qualitative theory of Hughes and Ingold[41] or simple electrostatic theory[42a] predicts rate enhancement in less polar solvents.[42b] Such a transition state is depicted in eq 9. Related reactions which appear to proceed *via* mechanisms that show predominant unimolecular character as in the hydrolysis of phosphate monoester dianions[29] and the

$$R-\overset{+}{N}H_2-P\overset{O}{\underset{O^-}{\big\backslash}}O^- \longrightarrow \left[R-\overset{\delta+}{N}H_2\cdots P\overset{O}{\underset{O^-}{\big\backslash}}O^{\delta-} \right] \longrightarrow \text{products} \quad (9)$$
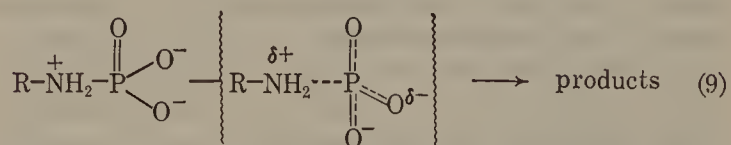
hydronium ion catalyzed hydrolysis of sulfate monoesters are accelerated by organic solvents.[43] The effect of mixed solvents on k_{obsd} should vary, however, with the nature of the phosphoramidate since K_{zw} and the degree of charge neutralization are expected to roughly

(36) Recent studies by Hamer [N. K. Hamer, *J. Chem. Soc.*, 404 (1966)] on monoesterified phosphoramidic acids derived from N-phenylethylenediamine and 2-aminobenzylamine have failed to disclose intramolecular attack by the vicinal amino group. These results have been interpreted to signify the need for a linear transition state which cannot be accommodated through five- or six-membered ring formation. However, it appears premature to rule out (7c) on this basis at present.

(37) M. L. Bender and J. M. Lawlor, *J. Am. Chem. Soc.*, **85**, 3010 (1963).

(38) S. J. Benkovic, *ibid.*, **88**, 5511 (1966).

(39) J. T. Edsall and M. H. Blanchard, *ibid.*, **55**, 2337 (1933).

(40) Since $v = k_r[RNH_2^+–PO_3^{2-}]$, where $[RNH_2–PO_3H^-] = [RNH_2^+–PO_3^{2-}] + [RNH–PO_3H^-]$ and $K_{zw} = [RNH_2^+–PO_3^{2-}]/[RNH–PO_3H^-]$, $k_{obsd} = k_r K_w/(K_{zw} + 1)$. In the above case $K_{zw} < 1$ is assumed. A similar postulation has been offered by Chanley and Feageson in the hydrolysis of N-arylphosphoramidates.

(41) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, p 346.

(42) (a) K. Wiberg, "Physical Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1964, p 374. (b) The above solvent theories must be applied with caution. Solvolyses of phosphate monoester dianions which are to a high degree unimolecular generally, as predicted, are accelerated by nonpolar solvents. Exceptions, however, are known.[29]

(43) B. D. Batts, *J. Chem. Soc.*, 547, 551 (1966).
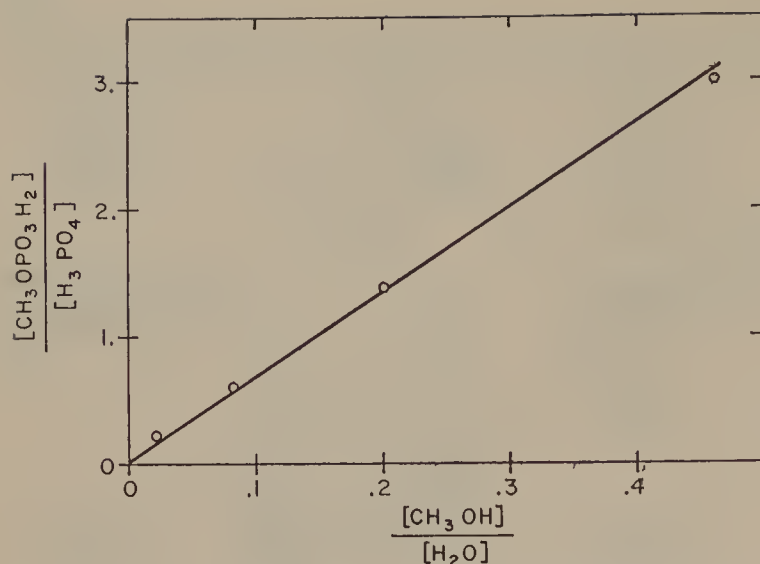
Figure 5. Plot of the ratio of methyl phosphate–orthophosphoric acid concentration against the ratio of methanol–water concentration for *o*- and *p*-carboxyphenyl phosphoramidates at $\mu = 0.2$, 35°. Ordinate values are averages of mole fractions $CH_3OPO_3H_2$ observed over pH 2–8 at various methanol concentrations for both compounds.

correlate with the pK_a' of the amino group. Since $K_{zw} > 1$ for phosphoramidate, k_{obsd} is independent of a solvent effect on K_{zw}[11] and presumably only reflects a kinetic solvent effect which results in *ca.* a 20% increase in k_{obsd} in 50% dioxane–water. The species [HOOC–RNH$_2^+$–PO$_3^{2-}$] may hydrolyze, at least partially, *via* a bimolecular pathway and reflect both a change in K_{zw} and the decrease in water concentration. Consistent also with a pathway unimolecular in character is the fact that $\Delta S^{\ddagger}$ for both *p*-chlorophenyl phosphoramidate and phosphoramidate itself is -6.3 and -1.6, respectively.

It is pertinent at this point to consider the product composition in alcohol–water mixtures. In the solvolysis of both anionic species for either **1** or **2**, a marked preference for the alcohol component is shown by the solvolytically important species. This may be expressed quantitatively by plotting the ratio of the mole fractions of alkyl phosphate to orthophosphoric acid against the ratio of mole fraction of alcohol to mole fraction of water. The slope, assuming the nonzwitterionic species does not undergo solvolysis, is simply the relative selectivity of the phosphoramidate for alcohol. Figure 5 is such a plot for the methanol–water mixtures, and applies to *all* species for both **1** and **2**, since the mole fraction methyl phosphate is invariant over the pH range 2–8. The selectivity for methanol is eightfold greater than that for water. Similar calculations for ethanol, 2-propanol, and *t*-butyl alcohol show the selectivity for alcohol is *ca.* four-, two-, and twofold, respectively.[44] On chemical grounds it seems reasonable to assume that the solvolysis products arise from the reactions of the zwitterionic species. One cannot rule out at present a contribution from solvolysis of the nonzwitterionic form on the basis of the above pH–rate profiles in mixed solvents. However, experiments in 5% methanol–water where the solvolytic contribution of the nonzwitterionic species should be minimal yield the same

ratio of methyl phosphate:orthophosphoric acid as mixed solvents 53% by volume in methanol. Assuming that the partitioning of the nonzwitterionic species to solvolytic products differs from the zwitterionic form, one may argue that the zwitterionic species is the active species in the solvolysis reactions.

It appears, therefore, that the collective data do not support a "free metaphosphate" intermediate in the hydrolysis of the anionic species since the former is predicted to be nonselective. A similar conclusion has been reached on the basis of solvent composition studies in the electrophilic-catalyzed hydrolysis of phosphoramidate monoanion,[13] whereas its hydrolysis has been viewed as being bimolecular.[11] The bimolecular postulation was based on the fact that both k_{obsd} and the product composition in methanol–water mixtures could be correlated with a bimolecular rate expression since k_{obsd} increased with increasing methanol concentration in these mixtures. Indeed it is possible that the noncatalyzed hydrolysis of phosphoramidate has a greater degree of bimolecular character due to a more basic leaving group. In **1** and **2** no such correlation is observed, the leaving group is less basic, and this bimolecular aspect disappears. The selectivity of the monoanionic species of both phosphoramidate and *p*-chlorophenyl phosphoramidate for methanol is *ca.* eightfold and therefore similar to that observed for **1** and **2**. It is noteworthy that catalysis by the neighboring carboxyl group does not alter the product composition; the same is true in the catalyzed and noncatalyzed hydrolysis of phosphoramidate. This phenomena is most readily explained in unimolecular terms. On the other hand the partial bimolecular character of the solvolysis of **1** and **2** is manifested by the phosphorylation of 2-propanol, a synthesis which is not observed in the solvolysis of aromatic monoester monoanions where nonselective phosphorylation is the generally observed case. Thus it appears that aryl phosphoramidate monoanions represent a situation where the transition state has both unimolecular and bimolecular character, and we prefer to view the transition state as featuring a long P–N bond with little bond formation between phosphorus and the incoming nucleophile. The unusual features of this transition state are probably in part due to the availability of vacant d orbitals on phosphorus. Insofar as the attack of nitrogen nucleophiles is applicable to alcohols, the slope of the Brønsted plot (0.22) for the reaction of a series of pyridines with phosphoramidate monoanion indicates little bond formation between the incoming nucleophile and phosphorus.

Neutral Species. Inspection of the pH–rate profiles for **1** and **2** indicate that $k_1(\mathbf{1}) > k_1(\mathbf{2})$. This may result from the operation of one of several possible mechanistic modes that include general acid catalysis, intramolecular phosphoryl transfer, or electrostatic catalysis (eq 10a, c, and b, respectively). In addition to these and other related variations suggested for the anionic species, a steric acceleration of a bimolecular mechanism as noted in other *ortho*-substituted reagents is possible.[45]

It seems reasonable to postulate the zwitterionic species as the active hydrolytic form, a hypothesis supported by the marked depression (*ca.* fivefold) of k_1 in mixed solvents. A similar phenomenon has been ob-

(44) The value of the selectivity ratio for ethanol–water mixtures was calculated from the average product composition at pH >2 for solvolysis of **1** and **2**; for 2-propanol and *t*-butyl alcohol–water mixtures the value was computed from the average product composition at pH >2 for solvolysis of **2**.

(45) R. W. Taft, "Steric Effects in Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1956, Chapter 3.

$$\text{(10)}$$
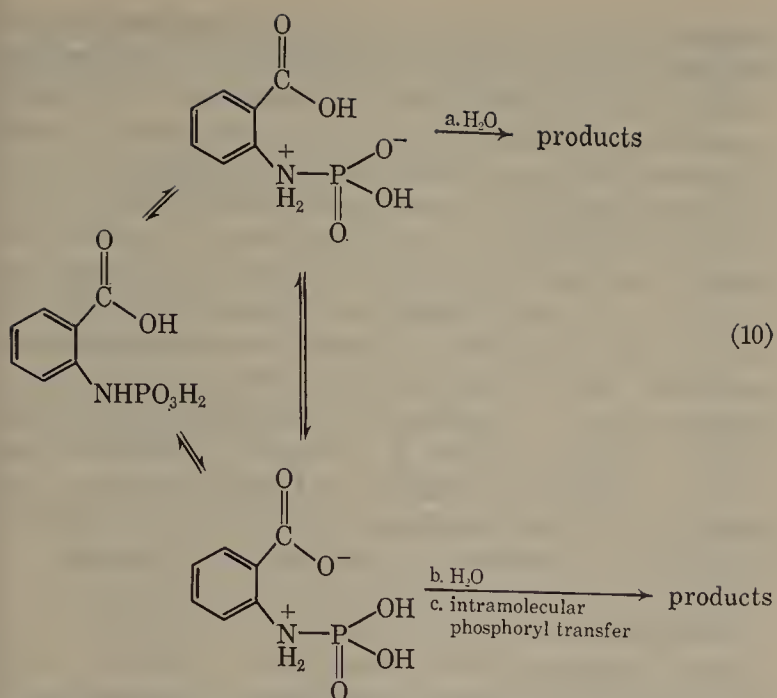
served by Chanley in the solvolyses of N-arylphosphor-amidates which may be attributed to a decrease in K_{zw} and water concentration. On chemical grounds the formation of metaphosphate seems unlikely; thus the mechanisms in eq 10 are written as bimolecular. It is possible to form a protonated metaphosphate which should be at least as reactive as metaphosphate, but this is not borne out by the product composition studies.

Product composition studies in alcohol–water mixtures reveal that the selectivity of the neutral parallels that of the anionic species.[46] Although k_{obsd} is greater for the former, the ratio of k_{CH_3OH}/k_{H_2O} must be similar, again exhibiting a $ca.$ eightfold selectivity for methanol. The data of Chanley and Feageson may be interpreted in this manner with the result that the neutral species of phosphoramidate and p-chlorophenyl phosphoramidate exhibit a selectivity for methanol similar to 1 and 2.[46] It appears, therefore, that the relative insensitivity of phosphate and phosphoramidate monoanions may extend to the neutral species with the result that an anticipated small increase in β would be difficult to detect experimentally at low β values. It is also possible that the increased reactivity of the neutral relative to the monoanionic species may be generally due to a change in the Brønsted intercept rather than the slope as is found in the attack of nucleophiles on p-nitrophenyl phosphate dianion. This hypothesis remains to be tested further experimentally. Solvolysis of the neutral species, however, is more sensitive to probable steric effects since t-butyl alcohol and 2-propanol–water mixtures phosphorylate 2 but not 1 at pH's where the neutral species predominates. Thus, a bimolecular mechanism involving attack of the nucleophile on the zwitterion is favored. It is anticipated that the transition state for the neutral species features a shorter P–N bond than in the mono-anionic species. This is evidenced by an increased sensitivity to the above steric effect and the decrease in $\Delta S^{\ddagger}$ (-18.2 eu) found for phosphoramidate.

Hydronium Ion Catalysis. Both substrates are subject to hydronium ion catalysis, a general phenomena

for phosphoramidates. The greater value of $k_{H^+}(1)$ may be due to steric acceleration as found in the hydronium ion catalyzed hydrolysis of salicyl sulfate or general acid catalysis. Hydronium ion catalysis as expected is greater with the more basic substrate, phosphoramidate itself.

With the advent of hydronium ion catalysis, a slight drop in the mole fraction of methyl phosphate is observed. This parallels the observation of Chanley and Feageson[11] who extended their studies to higher acidities and demonstrated that the product composition for N-arylphosphoramidates approached that of the solvent. It seems doubtful that this arises from the formation of metaphosphate since a chemical driving force is lacking; on experimental grounds the solvolysis of the highly reactive triester, diisopropyl phosphorochloridate, in mixed ethanol–water solvents reveals that the relative reactivity of ethanol to water is only 1.22.[47] Thus we favor a bimolecular pathway involving attack by solvent on the protonated zwitterion.

$$\text{(11)}$$
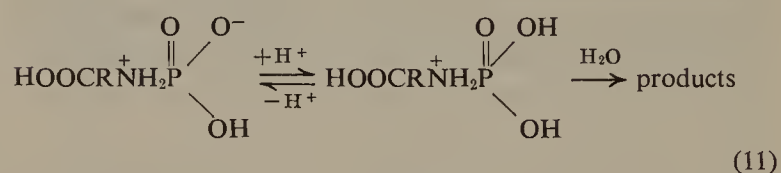
It is possible that solvent sorting is in some measure responsible for orthophosphoric acid formation since the proton donor is hydronium ion, and protonation and hydrolysis may be approaching a concerted process.

Summary

The hydrolysis of the o- and p-carboxyphenyl phosphoramidates appears to occur through a mechanistic gradation from a transition state predominantly unimolecular in character with the dianions to increasing bimolecular character with successive protonation. Kinetic studies reveal acceleration by the o-carboxyl group in the hydrolysis of several of the species. Product composition studies give no indication of free monomeric metaphosphate formation in the solvolysis of any of the species of either 1 or 2. Although the hydrolysis of the di- and monoanionic species appears to involve considerable unimolecular character, the intermediate species is a selective rather than nonselective phosphorylating agent. Thus the zwitterionic species involved in the solvolysis of 1 and 2 appears to be chemically similar to the presumed N-phosphoryl-pyridinium phosphorylating agent generated by the addition of pyridine to alcoholic solutions of phosphoramidate monoesters.[48] However, the synthetic utility of phosphoramidate monoesters to yield pyrophosphates in the presence of hydroxyl groups (solvent, dimethylformamide, no pyridine) may arise from a general acid catalyzed nucleophilic displacement of HPO_4^{2-} on the nonzwitterionic species of the phosphoramidate, the latter being greatly favored under the synthetic conditions employed.[49]

(46) There seems to be no reason to postulate that the products from alcohol–water mixtures at pH 2–3.5 do not arise from solvolysis of the neutral species. Calculations based on pK measurements in 53% methanol–water indicate that the neutral species will be present at $ca.$ 90% at pH 2. Although the rate of solvolysis of the neutral species is repressed in mixed solvents, it is still competitive with the solvolysis of the monoanions.

(47) I. Dostrovsky and M. Halmann, $J.$ $Chem.$ $Soc.,$ 502 (1953).
(48) The finding that solvolysis of methyl hydrogen cyclohexylphosphoramidate and phosphoramidate itself in the absence of pyridine yield predominantly orthophosphate in ethanol–water mixtures at 100° may arise from a difference in activation energies for ethanolysis $vs.$ hydrolysis. This may favor the former at elevated temperatures. See ref 10.
(49) A. Todd, $Proc.$ $Chem.$ $Soc.,$ 199 (1962).

Recently Kirby has postulated that the hydrolysis of aromatic phosphate dianions appears to proceed *via* formation of free monomeric metaphosphate.[29] It is important to note that the dianions in methanol–water mixtures yield consistently a product composition favoring methyl phosphate, whereas the monoanionic species more closely approximates the solvent composition. The authors rationalize this on the basis of selective solvation of the dianion. An alternate explanation is the possibility that the transition state does not involve free metaphosphate, although predominantly unimolecular in character. Treatment of the reported data in terms of the plot of Figure 5 reveals that 2,4-dinitrophenyl phosphate dianion is *ca.* fourfold more reactive with methanol than with water, consistent with considerable P–O fission in the transition state. Selective solvation cannot be completely eliminated nevertheless as a competing factor in the above and present study. It appears, however, that the nonselectivity criterion for metaphosphate is only satisfied at present in the solvolysis of phosphate monoester monoanions in methanol–water mixtures where there exists in addition a consider-able body of data supporting the metaphosphate hypothesis. In conclusion it should also be noted that the zwitterionic intermediates in phosphate monoester monoanion hydrolysis constitute the best leaving groups in terms of pK_a' arguments and probably delineate one end of the scale from bimolecular to unimolecular hydrolysis in phosphorus-containing esters. Moreover, in phosphoramidate hydrolysis in particular, one definitely appears to encounter transition states in which the extent of bond formation and fission are not directly proportional, which suggests that pentacovalent intermediates may be important in the hydrolysis of several of these species. From a biological standpoint the lability of phosphoramidates and their selectivity toward hydroxylic nucleophiles other than water indicate their utility as biochemical phosphorylating agents.

Chromic Acid Oxidation of Allyl Alcohols[1]

Sumner H. Burstein and Howard J. Ringold
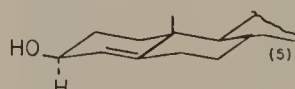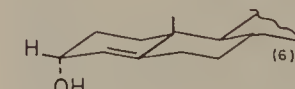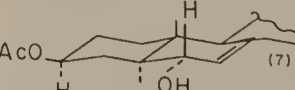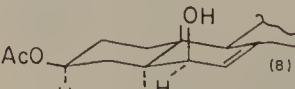
Contribution from the Worcester Foundation for Experimental Biology, Shrewsbury, Massachusetts 01545. Received March 6, 1967

Abstract: The rate-limiting step in the chromic acid oxidation of allyl alcohols is the cleavage of the carbon–hydrogen bond. In the absence of substantial strain factors equatorial alcohols are oxidized faster than the axial isomer, which may be rationalized on the basis of better overlap of the departing axial hydrogen. The rapid oxidation rate of unsaturated alcohols indicates a substantial contribution from α,β-unsaturated ketone resonance in the transition state.

In a previous publication,[2] evidence was presented that the conversion of allyl alcohols to the corresponding α,β-unsaturated ketones by dichlorodicyanoquinone (DDQ) oxidation proceeds *via* a rate-determining abstraction of hydride ion from carbon. In the case of a sterically compressed axial allyl alcohol, for example, the Δ^7-6β-ol **8**, DDQ oxidation of the axial alcohol was faster than oxidation of the equatorial counterpart **7**. However, the situation was reversed when the alcohols were relatively unhindered such as the Δ^4-3-ols **5** and **6** (Table I). These findings prompted us to determine the effect of unsaturation on chromic acid oxidation rates with these two isomeric alcohol pairs.

It has been demonstrated quite conclusively[3] that saturated secondary axial alcohols are oxidized more rapidly by chromic acid than the equatorial isomers and that these differences are magnified in sterically crowded situations. It is generally accepted[3,4] that rate en-

Table I. Relative Oxidation Rates of Allyl Alcohols with Dichlorodicyanoquinone[a]

	k_{rel}	$\dfrac{k_{eq}}{k_{ax}}$
(5)	33.7	
		6.4
(6)	5.2	
(7)	1.0	
		0.086
(8)	11.7	

[a] Reported in ref 2.

hancement in the latter case is due primarily to strain relief in the transition state which proceeds concomitantly with the development of carbonyl (trigonal) character. The primary deuterium isotope effect with

(1) Supported in part by Grant T-185, American Cancer Society.
(2) S. H. Burstein and H. J. Ringold, *J. Am. Chem. Soc.*, 86, 1952 (1964).
(3) J. Schreiber and A. Eschenmoser, *Helv. Chim. Acta*, 38, 1529 (1955).
(4) *Cf.* J. C. Richer, L. A. Pilato, and E. L. Eliel, *Chem. Ind.* (London), 2007 (1961).

Table II. Relative Oxidation Rates of Saturated and Unsaturated Alcohols with CrO_3 in 90% Acetic Acid–Sodium Acetate[a]

	k_{rel}	$\dfrac{k_{eq}}{k_{ax}}$		k_{rel}		$\dfrac{k_{eq}}{k_{ax}}$	$\dfrac{k_{unsatd}}{k_{satd}}$
HO... (1)	1.0		HO... (5)	R = H 310	R = D 45		310
		0.25				5.7	
H...OH (2)	4.0		R...OH (6)	54	11		13.5
AcO...OH (3)	1.4		AcO...OH (7)	130			93
		0.024				0.34	
AcO...OH (4)	58.0		AcO...OH (8)	380			6.6

[a] The kinetic procedure is detailed in the Experimental Section.

saturated carbinols is well known,[5] and together with other studies[6–8] has led to the formulation of an oxidation mechanism consisting of the reversible formation of a chromate ester which decomposes to the ketone plus a reduced form of chromium.[9] Usually, decomposition of the chromate ester has been found to be the slow step in the over-all reaction. However, in one instance,[8] a very severely hindered alcohol exhibited no isotope effect which indicated that it is possible for ester formation to become the rate-determining step.

Although it is well known[10] that allyl alcohols are rapidly oxidized by chromic acid, little study has been made of the effect, on reaction rate, of conformational and strain factors. One example of considerable interest was the finding that the 3β-equatorial alcohol of 3β,6β-dihydroxycholest-4-ene was oxidized more rapidly than the hindered axial 6β-ol.[11] This prompted the suggestion that the rate-determining step in the oxidation of allyl alcohols is the formation of an allyl carbonium ion rather than the cleavage of a carbon–hydrogen bond.

Table II lists the relative chromic acid oxidation rates for the Δ⁴-3-ols and their 3-deuterated analogs 5 and 6, the Δ⁷-6-ols 7 and 8, and the corresponding saturated compounds 1–4 which have been included for reference.[12] The oxidation rates were studied spectrophotometrically at 27° by following the disappearance of Cr^{VI} in 90% acetic acid which was 0.02 M in sodium acetate. The system was a pseudo-first-order one with steroid present in excess. The two saturated equatorial alcohols 1 (3β-hydroxy-5α-androstan-17-one) and 3 (3β-acetoxy-6α-hydroxy-5α-cholestane) exhibited very similar oxidation rates of 1.0

and 1.4, respectively. The saturated axial 3α-hydroxy compound 2 (3α-hydroxy-5α-androstan-17-one) with two diaxial hydrogen–hydroxyl interactions gave a relative oxidation rate of 4.0 while the 6β-hydroxy compound 4 (3β-acetoxy-6β-hydroxy-5α-cholestane) with a methyl–hydroxyl interaction in addition to two hydrogen–hydroxyl interactions reacted much faster (relative rate = 54).

Turning to the allyl alcohols, the equatorial 3β-ol 5 (3β-hydroxyandrost-4-ene) exhibited a rate of 310 times the saturated reference compound. The axial Δ⁴-3-ol 6 (3α-hydroxyandrost-4-ene), with a single hydrogen–hydroxyl interaction, had a relative rate of 54 and therefore was oxidized only 13.5 times faster than the saturated 3α-ol 2. Thus, just as in the DDQ reaction, chromic acid oxidation of the equatorial isomer proceeds faster than the axial isomer when the latter is relatively unhindered. The C-deuterated analogs of 5 and 6 were also studied and gave substantial isotope effects: k_H/k_D (eq) = 6.9; k_H/k_D (ax) = 4.9. On the basis of the isotope effect, it is clear that the rate-limiting step in the chromic acid oxidation of allyl alcohols is indeed the cleavage of the carbon–hydrogen bond. Also, there is no reason to doubt that the general mechanism involving the prior formation of a chromate ester applies for unsaturated as well as saturated alcohols.

Introduction of a 7,8 double bond into the 6-hydroxy compounds gave rate increases that were not so pronounced as with the 3-alcohols, although a similar equatorial–axial pattern was maintained. The equatorial alcohol 7 (3β-acetoxy-6α-hydroxy-5α-cholest-7-ene) had a relative rate of 130 which was 93 times the saturated analog 3. The axial isomer 8 (3β-acetoxy-6β-hydroxy-5α-cholest-7-ene) with one methyl–hydroxyl and one hydrogen–hydroxyl interaction exhibited a rate of 380 for an enhancement of 6.6 times the saturated compound 4. By comparing 8 vs. 6, it is obvious that the introduction of steric strain into the allylic alcohols leads to an enhanced chromic acid oxidation rate. However the strain factor is considerably more important in the saturated substances 4 vs. 2.

The most striking effect in the unsaturated alcohols is the great oxidation rate of the equatorial isomers which is completely unrelated to strain or strain release. The explanation which was invoked[2] to explain similar

(5) F. H. Westheimer and N. Nicolaides, *J. Am. Chem. Soc.*, **71**, 25 (1949).
(6) F. H. Westheimer and A. Novick, *J. Chem. Phys.*, **11**, 506 (1943).
(7) F. Holloway, M. Cohen, and F. H. Westheimer, *ibid.*, **73**, 65 (1951).
(8) J. Rocek, F. H. Westheimer, A. Eschenmoser, L. Moldovanyi, and J. Schreiber, *Helv. Chim. Acta*, **45**, 2554 (1962).
(9) K. B. Wiberg and H. Schafer, *J. Am. Chem. Soc.*, **89**, 455 (1967).
(10) G. Grimmer, *Ann. Chem.*, **636**, 42 (1960).
(11) L. F. Fieser, *J. Am. Chem. Soc.*, **75**, 4377 (1953); L. F. Fieser and M. Fieser, "Steroids," Reinhold Publishing Corp., New York, N. Y., 1959, pp 203, 225.
(12) Our results for the saturated carbinols agree qualitatively with those reported by Schreiber and Eschenmoser,[3] who report relative rates of 1.0, 3.0, 2.0, and 36 for compounds 1–4. Numerical differences may be due to the fact that our runs were made in the presence of sodium acetate while the others were unbuffered.

effects in the DDQ oxidation of allyl alcohols may be applied to the chromic acid oxidation. We believe the important factor is not that the alcohol is equatorial but rather that the hydrogen being removed in the rate-determining step is axial, which permits continuous overlap with the π electrons of the adjacent double bond (*i.e.*, the resonance interaction between the incipient carbonyl group and the double bond is maximal). Although it is not known in the chromic acid case whether hydrogen is removed from carbon as a proton or as hydride, the same steric requirements for overlap pertain in either case. The general similarity of k_{eq}/k_{ax} ratios in the DDQ oxidation (Table I) and chromic acid (Table II) is consistent with hydride loss in chromic acid oxidation but does not permit exclusion of a proton abstraction mechanism, in particular, if the reaction is a concerted cyclic process.

The Eschenmoser steric-strain relief hypothesis has been challenged[13] in the past on the grounds that in the transition state almost a fully developed carbonyl would be required to explain some of the observed rate accelerations. While better overlap explains the difference between equatorial and axial allyl alcohol oxidation rates, it must be recognized that the basic factor in the rapid oxidation of the allyl alcohols is the resonance contribution of the incipient α,β-unsaturated ketone.[14] Obviously this requires significant ketonic character in the transition state and may be cited in support of the Eschenmoser hypothesis. Also, based on these principles, it may be anticipated that un-saturated alcohols which yield *S-trans*-unsaturated ketones will be oxidized more readily than those which lead to *S-cis*-unsaturated ketones due to the more favorable resonance contribution of the former. It is probable that the selective oxidation of the 3β-alcohol of 3β,6β-dihydroxycholest-4-ene[11] stems primarily from this latter factor.

Experimental Section

A. Materials. Glacial acetic acid, chromium trioxide, and sodium acetate were commercially available analytical grade substances and were not purified further. 3β-Hydroxy-5α-androstan-17-one (**1**) and 3α-hydroxy-5α-androstan-17-one (**2**) were obtained from commercial sources and their melting point and chromatographic homogeneity used as criteria of purity. Preparation of the Δ⁴-3-ols **5** and **6** has been previously described.[2]

3β-Acetoxy-6α-hydroxy-5α-cholestane (**3**). The procedure was a slight modification of the preparation reported by Nussim, *et al.*[16] Cholesterol acetate (1 g) was dissolved in dry ether and a 25-fold excess of gaseous diborane was passed into the solution at 0° for a period of 30 min. The diborane was generated in a separate vessel by the slow addition of sodium borohydride in diglyme to a diglyme solution of boron trifluoride etherate. The steroid reaction mixture was allowed to warm to room temperature over a 30-min period, and the organoborane then cleaved by shaking the ethereal solution with 1% sodium hydroxide containing hydrogen peroxide and separating the phases as soon as possible. The ether extract was washed with water and ferrous sulfate solution, dried over sodium sulfate, and evaporated. Chromatography of the residue on neutral alumina (15 g, activity III) gave the desired compound in the benzene–cyclohexane (1:1) eluate. Crystallization from aqueous acetone gave 130 mg of pure material, mp 138–139°,

which was homogeneous on thin layer silica gel chromatography. In the infrared (CHCl₃), the compound showed acetate bands at 5.81 and 8.03 μ. Saponification for 1 hr with 1% potassium hydroxide in hot methanol gave the authentic diol, mp 220° (lit.[15] mp 217°).

3β-Acetoxy-6β-hydroxy-5α-cholestane (**4**). A cold solution of 1 g of 3β-acetoxy-5α-cholestan-6-one in 50 ml of tetrahydrofuran was treated with a solution of 1 g of sodium borohydride in 5 ml of water. The mixture was stirred for 16 hr at room temperature and then added with stirring to an ice-cold solution of dilute hydrochloric acid. The precipitate was filtered, washed, dried, and twice crystallized from aqueous acetone to yield 500 mg of desired mono-acetate, mp 156–158°. In the infrared, acetate bands were visible at 5.81 and 7.95 μ. Thin layer chromatography on silica gel (ethyl acetate–benzene 1:9) showed only a single spot. Acetylation with acetic anhydride–pyridine gave the diacetate, mp 135–137° (lit.[16] mp 139°), and saponification as described above gave the free diol, mp 190° (lit.[17] mp 192°). On silica gel thin layer plates, **3** and **4** exhibited R_f values of 0.56 and 0.64, respectively (hexane–acetone 3:2).

3β-Acetoxy-6α-hydroxy-5α-cholest-7-ene (**7**). 7-Dehydrocholesterol acetate (1 g) was hydroborated by the procedure described above except that the total reaction time was 45 min at 0°. The crude product was chromatographed on 15 g of neutral alumina and the desired product eluted with benzene–methanol (98:2). Crystallization from aqueous acetone gave 240 mg of **7**, mp 143–144°, homogeneous on silica gel thin layer chromatography. The compound had acetate bands at 5.81 and 7.9 μ in the infrared. In the nmr,[18] the C-7 vinylic proton was unsplit by the C-6 proton and appeared as a singlet at 311 cps, consistent with a dihedral angle of approximately 90°. The acetate methyl was at 122 cps and the 19-methyl group at 52 cps. Saponification of **7** gave the known diol of mp 192°.[19]

3β-Acetoxy-5α-cholest-7-en-6-one. A solution of **6** (500 mg) in acetone (100 ml) was cooled to 15° and treated dropwise with 1.1 equiv of chromic acid in sulfuric acid. Methanol was added to destroy excess chromic acid and water added to precipitate the product. The solid was crystallized from aqueous methanol to yield 420 mg of 6-ketone, mp 148–150° (lit.[20] mp 151°); λ_{max}^{EtOH} 244 mμ (ε 12,700); ν_{max}^{KBr} 5.79, 6.01, 6.19, and 8.08 μ.

3β-Acetoxy-6β-hydroxy-5α-cholest-7-ene (**8**). The 6-keto compound (above) was reduced with sodium borohydride as described for the preparation of **4** and gave after crystallization from aqueous acetone a 78% yield of the desired 6β-ol, mp 156–157°. On silica gel thin layer chromatography (hexane–acetone 3:2), compound **8** was homogeneous and slightly less polar than the equatorial isomer; ν_{max}^{KBr} 2.84, 5.76, 5.83, and 7.97 μ; nmr doublet 324, 328.5 cps (C-7 H), 122 cps (acetate CH₃), 60 cps (19-CH₃).

B. Kinetic Determinations. The rates of oxidation were measured at 27° and followed spectrophotometrically as described in the literature.[3,10,13] Reactions were carried out directly in a 3-ml cuvette which was maintained at the required temperature by means of a thermostated cell compartment. The disappearance of the Cr^VI maximum at 340 mμ was used to follow the course of reaction and measurements were made on a Zeiss PMQ-II instrument. The medium was 90% acetic acid which was 0.02 M in sodium acetate. Reactions were run as "pseudo first order"[13] by using steroid concentrations in the ratio of 10 moles to 1 mole of chromium trioxide.

Rate curves were plotted as log optical density *vs.* time and the best straight line was drawn through the series of observed points. From these curves, second-order rate constants were calculated by substitution into the equation

$$k = \frac{1}{(a-b)t} \ln\left[\frac{b(a-x)}{a(b-x)}\right] \cong \frac{1}{(a-b)t} \ln\left(\frac{b}{b-x}\right)$$

where a = initial steroid concentration, b = initial CrO₃ concentra-

(13) H. Kwart and P. S. Francis, *J. Am. Chem. Soc.*, **81**, 2116 (1959); H. Kwart, *Chem. Ind.* (London), 610 (1962).

(14) Although higher steady-state concentration of the chromate ester would also lead to a faster over-all rate, there is no reason to believe that the equilibrium position for ester formation would markedly differ in the saturated and unsaturated compounds.

(15) M. Nussim, Y. Mazur, and F. Sondheimer, *J. Org. Chem.*, **29**, 1121 (1964).

(16) Pl. A. Plattner, Th. Petrzilka, and W. Lang, *Helv. Chim. Acta*, **27**, 513 (1944).

(17) R. E. Marker and J. Kreuger, *J. Am. Chem. Soc.*, **62**, 79 (1940).

(18) The nmr spectra were obtained on a Varian Model A-60 spectrophotometer at 60 Mcps. All spectra were run in deuteriochloroform with tetramethylsilane as internal standard and are reported as cps downfield from the reference compound.

(19) L. Caglioti, G. Cainelli, and G. Maina, *Tetrahedron*, **19**, 1057 (1963).

(20) C. Djerassi, J. C. Knight, and H. Brockman, Jr., *Chem. Ber.*, **97**, 3118 (1964).

tion, and x = the amount of CrO_3 reacted at time t. All rates are expressed in Table II relative to 3β-hydroxy-5α-androstan-3-one (1) which had a second-order rate constant of 2.80×10^{-3} l. mole^{-1} sec^{-1}.

The reactions were initiated by mixing nine parts of a freshly prepared solution of the steroid in glacial acetic acid with one part of an aqueous solution of chromium trioxide which was 0.20 M in sodium acetate. In the case of the slower reactions, the steroid was 30.9×10^{-3} M and chromic acid 3.09×10^{-3} M. In the faster reactions, the concentrations were 30.9×10^{-4} and 3.09×10^{-4} M, respectively. All reactions were allowed to proceed for at least one half-life. With one exception the steroidal substrates were stable in acetic acid over the period of measurement and no side reaction would be detected by product analysis. In the case of 3α-hydroxy-androst-4-ene (6) and the corresponding deuterio compound, a small amount of dehydration was noted. However, this side reaction was insufficient to cause noticeable deviation in the pseudo-first-order plot. All substrates were run in duplicate or triplicate.

Sulfoxide–Carbodiimide Reactions. V.[1]
Reactions of 2,6-Disubstituted Phenols

M. G. Burdon[2] and J. G. Moffatt

*Contribution No. 38 from the Institute of Molecular Biology,
Syntex Research, Palo Alto, California. Received March 29, 1967*

Abstract: Phenols substituted in the 2 and 6 positions with alkyl groups react with dimethyl sulfoxide and dicyclohexylcarbodiimide in the presence of anhydrous phosphoric acid to give 2,6-disubstituted 6-(thiomethoxymethyl)cyclohexa-2,4-dien-1-ones. These dienones tend to rearrange to thiomethoxymethylphenols during silica chromatography or upon addition of acids, and studies designed to elucidate the mechanism of these rearrangements are described. Under suitable conditions the thiomethoxymethyl group can be efficiently transferred from a suitably substituted dienone to another acceptor molecule. *o*-Chlorophenols behave unusually and lead primarily to 1,3-benzoxathians.

Following the development of the mild, but efficient, dimethyl sulfoxide–dicyclohexylcarbodiimide (DMSO–DCC) method for the oxidation of hydroxyl groups[3] we have undertaken a general program studying the reactions of these reagents with other functional groups. In part IV of this series[1] we have described the mild, acid-catalyzed reactions of DMSO and DCC with a variety of phenols containing unsubstituted *ortho* positions. Such reactions led to a number of different types of products depending upon the nature of the starting material. The principal products were usually phenols substituted in one or both of the available *ortho* positions by thiomethoxymethyl groups (*e.g.*, 1), and frequently low yields of products containing the previously undescribed 1,3-benzoxathian ring system (*e.g.*, 2) were also isolated. More strongly acidic phenols, such as nitrophenols, gave rise to aryl thiomethoxymethyl ethers (*e.g.*, 3), while thiophenols and naphthols were anomalous and gave diaryl disulfides and bis(thiomethoxymethyl)dihydronaphthalenones (*e.g.*, 4), respectively. Comparable products were also found using sulfoxides other than DMSO.

Mechanisms were proposed for these various reactions[1] involving initial attack of the phenolic oxygen upon the DMSO–DCC adduct 5 which has been shown by isotopic experiments[3d] to be the first intermediate

during oxidation of alcohols. The *ortho*-alkylation reaction then proceeds *via* the aryloxysulfonium salt 6 and the sulfonium ylide 7, the carbanion of which intramolecularly alkylates the available *ortho* position, giving the phenol 9 *via* the dienone 8.
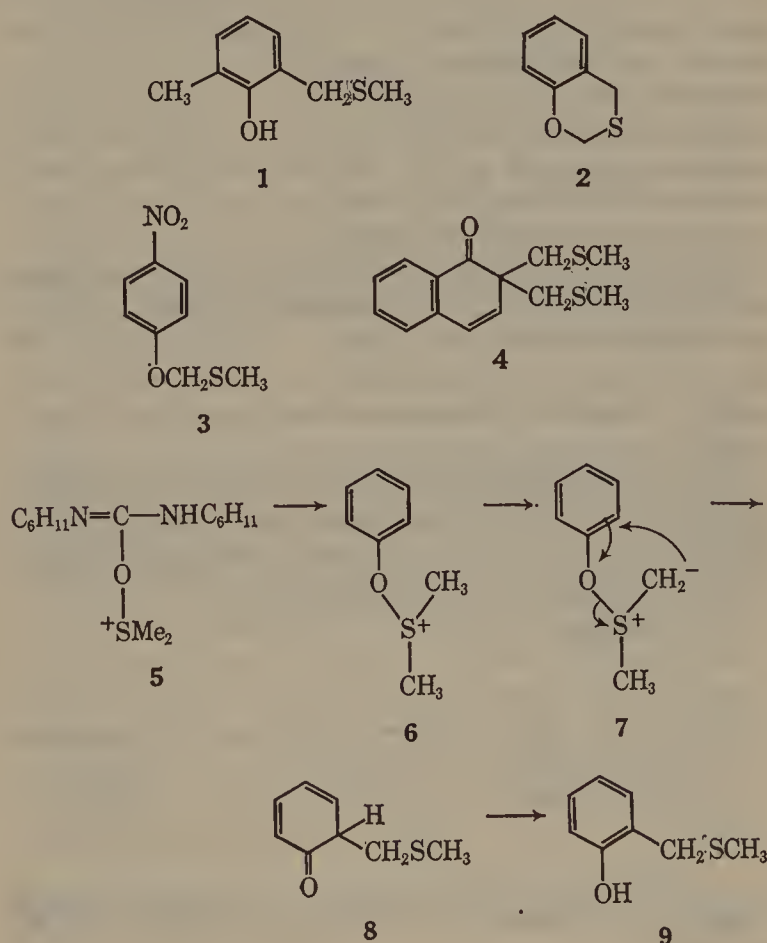
(1) For part IV see M. G. Burdon and J. G. Moffatt, *J. Am. Chem. Soc.*, 88, 5855 (1966).

(2) Syntex Postdoctoral Fellow, 1964–1965, and recipient of a Wellcome Trust travel grant, for which we express our thanks.

(3) (a) K. E. Pfitzner and J. G. Moffatt, *J. Am. Chem, Soc.*, 85, 3027 (1963); (b) K. E. Pfitzner and J. G. Moffatt, *ibid.*, 87, 5661 (1965); (c) K. E. Pfitzner and J. G. Moffatt, *ibid.*, 87, 5670 (1965); (d) A. H. Fenselau and J. G. Moffatt, *ibid.*, 88, 1762 (1966).

Very recently a brief paper by Torssell[4a] has questioned the free existance of the alkoxysulfonium compound[3b,d] analogous to **6** during oxidation of alcohols with the DMSO–DCC reagent. Further experimental details and study are necessary in order to assess this suggestion, but the possibility should not be excluded that the *ortho*-alkylation reaction may also proceed *via* a termolecular intermediate such as **10**. For convenience in the subsequent discussion we will continue to assume that the aryloxysulfonium compound **6** does indeed exist free since the Torssell mechanism differs from ours only in the intimate details of the proton-abstraction step.
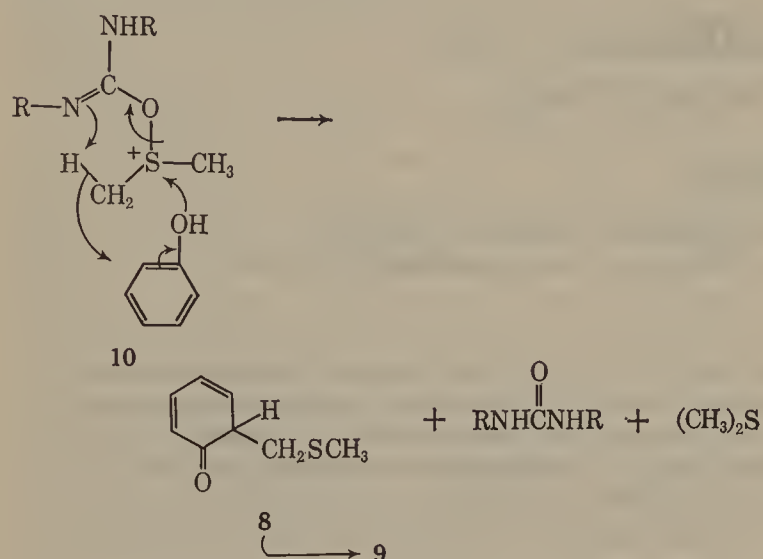
2,6-Disubstituted phenols would also be expected to react with the sulfonium pseudourea **5**, and the results of a number of such examples are reported in this paper. A preliminary report of part of this work has appeared,[5a] and some related observations have been briefly described by Pfitzner, *et al.*[5b]

Upon addition of anhydrous orthophosphoric acid (0.5 equiv) to a solution of 2,6-dimethylphenol (1 equiv) and DCC (3 equiv) in a mixture of DMSO and benzene an exothermic reaction took place and dicyclohexylurea was deposited. Thin layer chromatography indicated that within 30 min no starting material remained and a single ultraviolet-absorbing spot resulted. Following extraction of the DMSO with water the organic solvent soluble products were chromatographed on a column of silicic acid, giving a crystalline product identified as 2,6-dimethyl-4-(thiomethoxymethyl)phenol (**11**) in 66% yield. The structure of **11** was confirmed by its elemental analysis and also by its nuclear magnetic resonance (nmr) spectrum which

showed the presence of a thiomethoxymethyl group as two singlets at 118 (SCH_3) and 214 cps ($ArCH_2S$). The product was phenolic (ultraviolet and infrared spectra) and its symmetrical nature was demonstrated by the appearance of two aromatic protons as a sharp singlet at 415 cps in the nmr spectrum. Desulfurization with a sponge nickel catalyst[6] led to the rapid and quantitative formation of crystalline 2,4,6-trimethylphenol, mp 72–73°, which was indistinguishable from an authentic sample. The formation in high yield of the *p*-(thiomethoxymethyl)phenol is in direct contrast with the exclusive formation of *o*-(thiomethoxymethyl) products arising from phenols containing unsubstituted *ortho* positions.[1]

A similar reaction with 2,4,6-trimethylphenol once again led to the very rapid consumption of all the starting material and formation of a single ultraviolet-absorbing spot on thin layer chromatograms. Silica column chromatography gave a high yield of a crude material which ran as an elongated spot on thin layer chromatography and from which crystalline 2,4,6-trimethyl-3-(thiomethoxymethyl)phenol (**12**) was obtained in moderate yield. The crystalline material gave the expected analysis (Table I) and spectral data (Table II) and the mother liquors were clearly a mixture of **12** and another product with λ_{max} 320 mμ (30% **12** by vapor phase chromatography) that will be discussed shortly. Desulfurization of **12** gave crystalline 2,3,4,6-tetramethylphenol, mp 77–78°.

Reexamination by vapor phase chromatography of the crude, extracted reaction mixtures from 2,6-dimethylphenol and 2,4,6-trimethylphenol showed that in each case *none* of the previously isolated thiomethoxymethylphenols (**11** and **12**) was present. The only detected products were excess DCC and a single major peak in each reaction, together with trace amounts of unreacted starting material. Following chromatography of this crude mixture from 2,6-dimethylphenol on a column of silicic acid, however, the previously isolated, crystalline 2,6-dimethyl-4-(thiomethoxymethyl)phenol (**11**) was once again isolated in excellent yield. Accordingly, **11** must not be a primary product of the reaction but rather the consequence of a facile chemical change occurring during chromatography. This situation became clear when it was observed that very rapid chromatography of the crude reaction mixture from 2,6-dimethylphenol on preparative 1-m-long glass plates with a 1.3-mm-thick silica layer[7] (total time for application, development, and elution was less than 2 hr) permitted isolation of the original reaction product contaminated by only about 20% of **11** which could be selectively removed by extraction with dilute alkali. The nonalkali-extracted product was then distilled under high vacuum, giving a 66% yield of a yellow oil which was shown to be 2,6-dimethyl-6-(thiomethoxymethyl)cyclohexa-2,4-dien-1-one (**13**). This compound, which was isomeric with **11**, was shown to be an unsaturated ketone by its infrared (ν_{max} 1650 cm^{-1}) and ultraviolet (λ_{max}^{MeOH} 308 mμ) spectra, and it rapidly rearranged to **11** upon addition of a trace of trifluoroacetic acid to its solution in methylene chloride. The nmr spectrum of **13** showed the pres-

(4) (a) K. Torssell, *Tetrahedron Letters*, 4445 (1966). (b) An alternative to the Torssell mechanism, suggested to us by a referee, involves addition of the phenol (or alcohol in the case of oxidation) to the adduct **5** with formation of the tetrasubstituted sulfur intermediate a which then collapses *via* a cyclic process directly to the sulfonium ylide **7** without intervention of the free sulfonium salt **6**.

(5) (a) M. G. Burdon and J. G. Moffatt, *J. Am. Chem. Soc.*, **87**, 4656 (1965); (b) K. E. Pfitzner, J. P. Marino, and R. A. Olofson, *ibid.*, **87**, 4658 (1965).

(6) Davidson Chemical Division of W. R. Grace and Co., Cincinnati, Ohio.

(7) H. Halpaap, *Chem. Ing. Tech.*, **35**, 488 (1963).

Table I. Physical Properties of Thiomethoxymethyl Compounds

Compd	Yield, %	Mp or bp[a] (mm), °C	Molecular formula	Calcd, % C	H	S	Found, % C	H	S
2,6-Dimethyl-4-TMM-phenol[b] (14)	66	40–42	$C_{10}H_{14}OS$	65.91	7.74	17.60	66.20	7.62	17.80
2,4,6-Trimethyl-3-TMM-phenol (12)	18	85–86	$C_{11}H_{16}OS$	67.32	8.22	16.35	67.41	8.16	16.50
2,6-Dimethyl-6-TMM-cyclohexa-2,4-dien-1-one (13)	66	60 (10⁻⁴)	$C_{10}H_{14}OS$	65.91	7.74	17.58	65.89	7.70	17.51
Dimer (14)	40	130–131	$C_{20}H_{28}O_2S_2$	65.91	7.74	17.58	66.17	7.55	17.44
2,4,6-Trimethyl-6-TMM-cyclohexa-2,4-dien-1-one (15)	93	65 (10⁻⁴)	$C_{11}H_{16}OS$	67.32	8.22	16.32	67.60	8.55	16.03
2,3,5,6-Tetramethyl-6-TMM-cyclohexa-2,4-dien-1-one (18)	86	90 (10⁻³)	$C_{12}H_{18}OS$	68.54	8.63	15.22	68.37	8.47	15.32
2,3,4,5,6-Pentamethyl-6-TMM-cyclo-hexa-2,4-dien-1-one (19)	85	80 (10⁻⁴)	$C_{13}H_{20}OS$	69.61	8.99	14.28	69.40	8.84	14.46
2,3,5,6-Tetramethyl-4-TMM-phenol (20)	93	144–145	$C_{12}H_{18}OS$	68.54	8.63	15.22	68.63	8.53	15.18
2,3,4,6-Tetramethyl-6-TMM-cyclohexa-2,4-dien-1-one (25) 2,4,5,6-Tetramethyl-6-TMM-cyclohexa-2,4-dien-1-one (26)	95	80 (10⁻³)	$C_{12}H_{18}OS$	68.54	8.63	15.22	68.90	8.86	14.62
2,4,5,6-Tetramethyl-3-TMM-phenol (27)	60	97–98	$C_{12}H_{18}OS$	68.54	8.63	15.22	68.84	8.57	15.17

[a] Boiling points refer to the bath temperature using a "Kugelrohr" short-path apparatus. [b] TMM refers to thiomethoxymethyl.

Table II. Spectral Properties of Thiomethoxymethyl Compounds

Compd	Ultraviolet spectra, λ_{max}, mμ (ϵ_{max}) MeOH	MeOH + KOH	Nmr spectra, cps SCH₃	ArCH₂S	Other
11	278 (1400)	255 (4500), 290 (1500)	118 (3, s)[a]	214 (2, s)	131 (6, s), 288 (1, s), 415 (2, s)
12	286 (2200)	290 (2000), 305 (sh) (700)	123 (3, s)	222 (2, s)	129 (3, s), 135 (3, s), 136 (3, s), 276 (1, s), 406 (1, s)
13	308 (3600)	Unchanged	122 (3, s)	162 (1, d, J = 12.5 cps) 182 (1, d, J = 12.5 cps)	72.5 (3, s), 113.5 (3, d, J = 1.5 cps) 370–420 (3, m)
14	241 (6800)	Unchanged	122 (3, s) 124 (3, s)	157 (2, s) 163 (2, s)	68 (3, s), 77 (3, s), 79 (3, s), 109 (3, s) 179 (1, d, J = 6 cps), 332 (1, q, J = 8 and 1.5 cps), 370–390 (2, m)
15	320 (3400)	Unchanged	121 (3, s)	159 (1, d, J = 13 cps) 179 (1, d, J = 13 cps)	71 (3, s), 113–117 (6, m) 356 (1, q), 405 (1, q)
18	325 (4650)	Unchanged	119 (3, s)	167 (1, d, J = 12 cps) 191 (1, d, J = 12 cps)	72 (3, s), 110–125 (9, m) 360 (1, s)
19	336 (4000)	Unchanged	117 (3, s)	169 (1, d, J = 12 cps) 190 (1, d, J = 12 cps)	70 (3, s), 110–130 (12, m)
20	278 (810), 284 (760)	283 (sh, 1150), 296 (sh, 500)	127 (3, s)	228 (2, s)	130 (3, s), 139 (3, s), 276 (1, s)
25 26	328 (3600)	Unchanged	121 (3, s)	178 (1, d, J = 12 cps) 158 (1, d, J = 12 cps) 188 (1, d, J = 12 cps) 169 (1, d, J = 12 cps)	358 (1, s) 405 (1, s) 117 (3, s), 113 (3, s) 112 (3, s), 69 (3, s)
27	288 (1800)	289 (1650), 307 (sh, 400)	125 (3, s)	225 (2, s)	129 (6, s), 135 (6, s), 276 (1, s)

[a] Integrated intensity and multiplicity; s, d, q, and m refer to singlet, double, quartet, and multiplet. Thus 129 (3, s) refers to a three-proton singlet at 129 cps. All nmr data in this table were obtained on a Varian A-60 spectrometer using solutions in deuteriochloroform, and are recorded in cycles per second downfield from an internal standard of tetramethylsilane.

ence of a S–CH₃ group as a singlet at 122 cps, a quaternary methyl group at 72.5 cps, a vinyl methyl group as a doublet at 113.7 cps (J = 1.5 cps), three vinyl protons between 370 and 420 cps, and the isolated CH₂S group as a pair of geminally coupled doublets (J = 12.5 cps) centered at 162 and 182 cps. Such a four-line pattern is typical of an isolated methylene group adjacent to an asymmetric center,[8] and the nature of the magnetic nonequivalence of the methylene protons has received considerable attention.[9] Storage of the pure dienone 13 at room temperature for even 1 day led to separation

of a white crystalline substance from which a pure isomer of the Diels–Alder dimerization product 14a or 14b could be obtained. The analogous spontaneous dimerization of 6,6-dimethylcyclohexa-2,4-dien-1-one and related compounds has previously been described.[10] No clear preference for structure 14a or 14b can be inferred from spectral data, and the broad melting point range of the crude product suggests that perhaps both isomers were originally formed. Dipole moment measurements, which have been used previously[10b] to study the dimer from 2,6,6-trimethylcyclohexa-2,4-dien-1-one, have not been made. The infrared spectrum of 14 showed the presence of both conjugated

(8) (a) J. D. Roberts, "Nuclear Magnetic Resonance. Applications to Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1959, p 58; (b) E. I. Snyder, J. Am. Chem. Soc., 85, 2624 (1963), and references therein.

(9) L. Martin and G. J. Martin, Bull. Soc. Chim. France, 2117 (1966).

(10) (a) K. Alder, F. H. Flock, and H. Lessinich, Chem. Ber., 90, 1709 (1957); (b) T. L. Brown, D. Y. Curtin, and R. R. Fraser, J. Am. Chem. Soc., 80, 4339 (1958).

(ν_{max}^{KBr} 1675 cm^{-1}) and nonconjugated (ν_{max}^{KBr} 1715 cm^{-1}) carbonyl groups, and the ultraviolet spectrum was that of an α,β-unsaturated ketone (λ_{max} 241 mμ (ϵ 6800)). The dimeric nature of 14 was confirmed by mass spectrometry which showed an intense molecular ion (relative abundance 56%) at m/e 364. Other interesting features of this spectrum include: (1) the ready cleavage of the thiomethoxymethyl side chains as demonstrated by both the presence of an intense peak (relative intensity 100%) at m/e 61 corresponding to the methylmethylenesulfonium ion CH$_3$S=CH$_2^+$ and the presence of intense peaks at M − 60 (M − CH$_2$=S=CH$_2$) and M − 75 (M − CH$_2$=S=CH$_2$CH$_3$); (2) reversion of the dimer to the monomer (m/e 182, relative intensity 14%). Thermal cracking of 14 to the monomer 13 could also be demonstrated during distillation at 100° (10^{-4} mm) and by vapor phase chromatography whereby 13 and 14 gave apparently identical retention times. Alder[10a] has also noted thermal cracking of the 6,6-dimethylcyclohexa-2,4-dien-1-one dimer. The nmr spectrum of the dimer was completely in accordance with the proposed structures 14a or 14b and is summarized in Table II. The only unusual feature of this spectrum is that the methylene groups attached to sulfur unexpectedly appeared as singlets, rather than as pairs of doublets as in 13.

11   12   13

14a   14b
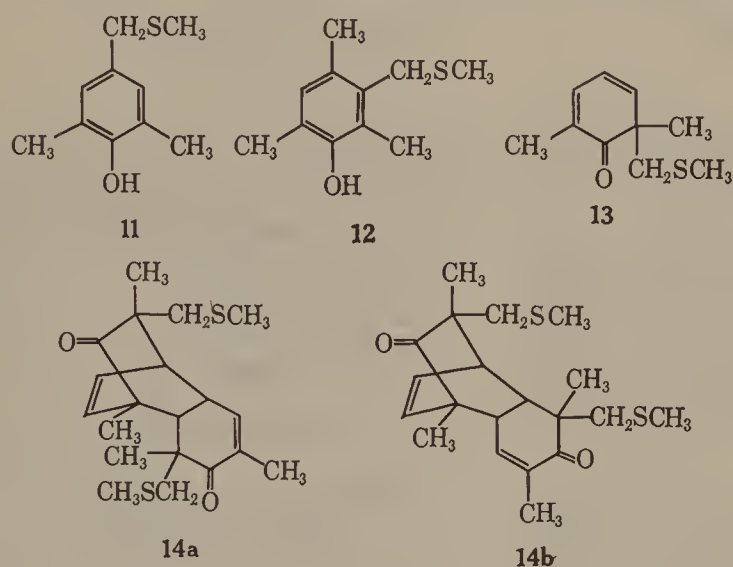
Chromatography of the pure ketone 13 on silicic acid columns, or storage of its solutions in the presence of silicic acid, led to complete rearrangement to the para-alkylated phenol 11. In a similar way addition of a trace of trifluoroacetic acid to a solution of 13 in methylene chloride led to almost instantaneous rearrangement to 11. The mechanism of this rearrangement is discussed later in this paper.

Rapid chromatography of the crude reaction products from 2,4,6-trimethylphenol on preparative silica plates led, in the same way, to the isolation of 2,4,6-trimethyl-6-(thiomethoxymethyl)cyclohexa-2,4-dien-1-one (15) in 93% yield. Unlike 13, this ketone showed little tendency to dimerize and was only partially isomerized (~40%) to the meta-alkylated phenol 12 upon overnight chromatography on a silicic acid column. Brief treatment with trifluoroacetic acid in methylene chloride (0.1 M), however, led to rapid rearrangement to 12. It is significant that it is exclusively the thiomethoxymethyl group which migrates, this being shown by comparison of the rearrangement product 12 (mp 85–86°) with the isomeric compound 2,4,5-trimethyl-6-

(thiomethoxymethyl)phenol (16), mp 51–53°, obtained previously[1] from the reaction of 2,4,5-trimethylphenol with DMSO and DCC. A related rearrangement of 6,6-dimethylcyclohexa-2,4-dien-1-one (17) to 2,3-dimethylphenol upon treatment with sulfuric acid in acetic anhydride has been previously described,[11] although, as will be seen later, the mechanism is probably quite different.

15   16   17
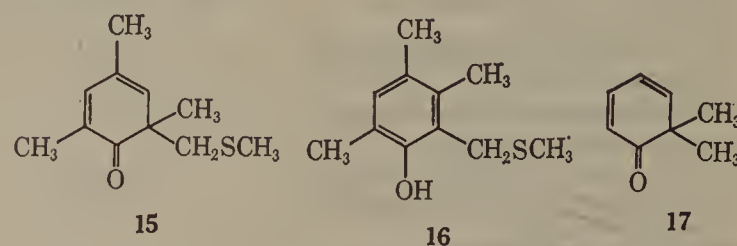
Similar reactions of DMSO and DCC upon 2,3,5,6-tetramethylphenol (durophenol) and 2,3,4,5,6-pentamethylphenol also led to the essentially quantitative formation of the cyclohexadienones 18 and 19 which were quite stable and could be chromatographed on columns of silicic acid without decomposition. Treatment of 18 with trifluoroacetic acid in methylene chloride or with one drop of concentrated hydrochloric acid in methanol led to an almost instantaneous rearrangement to 2,3,5,6-tetramethyl-4-(thiomethoxymethyl)phenol (20) which crystallized directly from the solvent. Desulfurization of 20 gave crystalline pentamethylphenol identical with an authentic sample. Treatment of 19 with hydrochloric acid in methanol led to a rapid conversion into pentamethylphenol. Further studies on these reactions are discussed later in this paper. Desulfurization of the dienones 18 and 19 was accompanied by reduction of the terminal double bond and gave, as the principal products isolated by preparative thin layer chromatography, 2,3,5,6,6-pentamethylcyclohex-2-en-1-one (21) and 2,3,4,5,6,6-hexamethylcyclohex-2-en-1-one (22), respectively, which were characterized by their ultraviolet (λ_{max} 245 mμ), infrared (λ_{max} 1660 cm^{-1}), and nmr spectra. A substantial amount of the intermediate product 23 which was reduced but not desulfurized was also isolated from the reaction of 18. In addition, the presence of nonultraviolet-absorbing, fully reduced products was apparent from thin layer chromatography, but these have not been further studied. No sign of the previously described 2,3,4,5,6,6-hexamethylcyclohexa-2,4-dien-1-one[12] was observed.

18   19   20

21   22   23
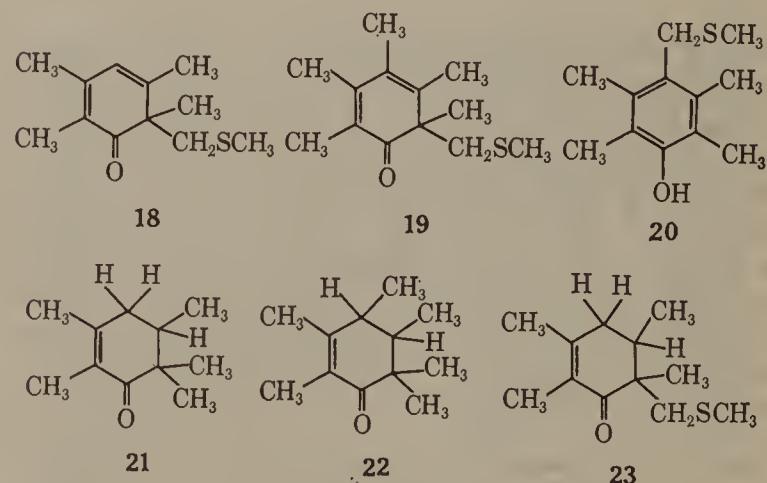
(11) (a) E. N. Marvel and E. Magoon, J. Am. Chem. Soc., 77 2542 (1955); (b) H. Budzikiewicz, Tetrahedron Letters, 12 (1960).
(12) H. Hart and R. M. Lange, J. Org. Chem., 31, 3776 (1966).

As might be expected, the reaction of 2,3,4,6-tetramethylphenol (24) led to a mixture of the two isomeric tetramethyl(thiomethoxymethyl)cyclohexadienones (25 and 26) which were indistinguishable by thin layer chromatography and barely resolved by vapor phase chromatography. The nmr spectrum of the mixture clearly showed it to consist of 60% of the less sterically hindered isomer 25 and 40% of 26, the single vinylic proton of 26 appearing at lower field than that of 25. The methylene groups of 25 and 26 also appeared as two overlapping, but clearly observable, quartets while the methyl groups were not resolvable. Treatment of the mixed ketones with acid led to a mixture of roughly equal amounts of the starting phenol 24 and 2,3,4,6-tetramethyl-5-(thiomethoxymethyl)phenol (27), the latter being identified by analysis and by desulfurization to pentamethylphenol. It therefore appears that the action of acid on ketone 25 leads to rearrangement of the thiomethoxymethyl group to the available *ortho* position while ketone 26 undergoes simple hydrolysis similar to that observed with 19.

24   25   26   27
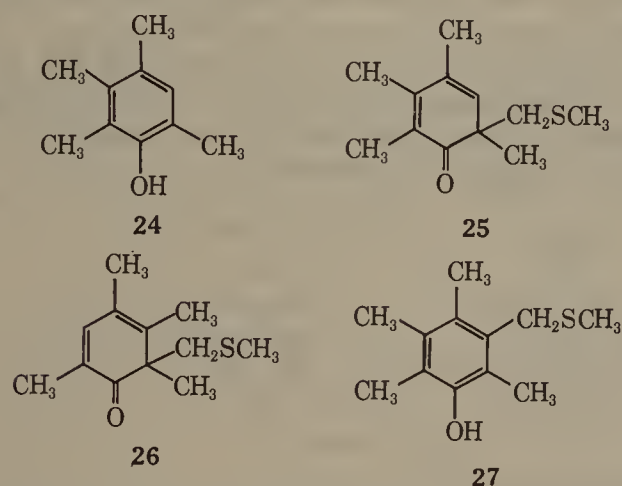
Since the (thiomethoxymethyl)cyclohexadienones (*e.g.*, 13, 15, and 18) may, with care, be isolated in almost quantitative yields, it appears almost certain that they are the exclusive intermediates in the formation of the *meta*- and *para*-alkylated phenols which we originally isolated following chromatography on silicic acid columns. The possible alternative alkylation of the phenol by the methylmethylenesulfonium ion (29), which could conceivably be generated by collapse of the ylide 28 derived from the DMSO–DCC adduct 5, seems to be ruled out by the complete inertness of anisole, 1,3-dimethoxybenzene, furan, and N,N-dimethylaniline under the usual reaction conditions. It has previously been shown that 1,3-dimethoxybenzene is alkylated by 29 derived from dimethylethoxysulfonium fluoroborate and triethylamine. The sulfonium compound 29 could also arise by expulsion of phenolate ion from the key phenoxysulfonium ylide intermediate 7. Such a process is also ruled out by the quantitative formation of the dienone 13, as shown by vapor phase chromatography, when 2,6-dimethylphenol is allowed to react with DCC,

28   29   7
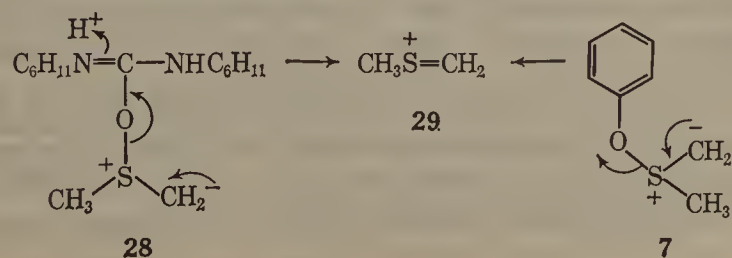
DMSO, and phosphoric acid in the presence of a tenfold molar excess of 1,3-dimethoxybenzene, anisole, or furan. No alkylation of these relatively nucleophilic additives was observed. As will be seen later, however, such compounds can be alkylated by transfer of a thiomethoxymethyl group from a dienone such as 19 in the presence of acid.

In order to cast light upon the mechanism by which the (thiomethoxymethyl)cyclohexadienones rearrange to *meta*- or *para*-alkylated phenols, we have studied the acid-catalyzed reactions of the ketone 18 derived from durophenol. We first checked whether the rearrangement of 18 to 20 was intra- or intermolecular by treating a mixture of 18 and 5 equiv of 2,6-dimethylphenol in methylene chloride with a trace of trifluoroacetic acid. The ketone 18 disappeared almost instantaneously and, in addition to 2,6-dimethylphenol and durophenol, the products were shown by quantitative vapor phase chromatography to be 67% 2,3,5,6-tetramethyl-4-(thiomethoxymethyl)phenol (20) and 33% 2,6-dimethyl-4-(thiomethoxymethyl)phenol (11).[13] Thus, even in the presence of a fivefold excess of another phenol, intramolecular rearrangement is favored by a factor of 2. A similar experiment using the dienone 13 from 2,6-dimethylphenol in the presence of 5 equiv of durophenol led to 75% intramolecular alkylation, giving 11, and 25% intermolecular reaction, giving 20.

The intramolecular rearrangements of (thiomethoxymethyl)cyclohexadienones could take place *via* a truly intramolecular cyclic process somewhat analogous to that operative in the *para* Claisen rearrangement[14] (path A) or by dissociation into the methylenemethylsulfonium ion and phenol followed by alkylation of the phenol at the nucleophilic *para* position (path B) if this is free.

Path A
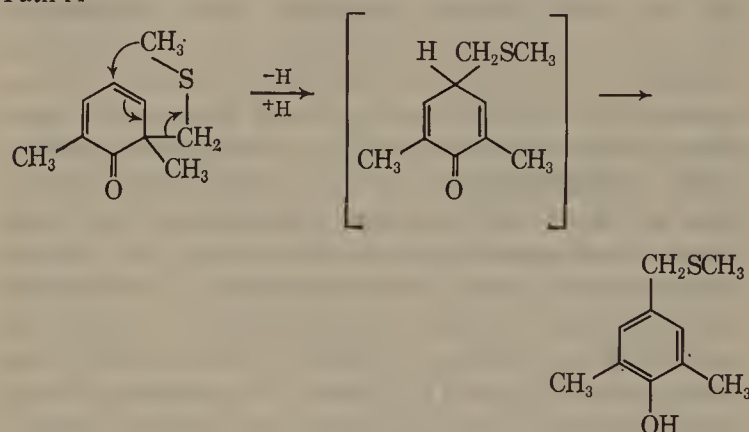
Path B
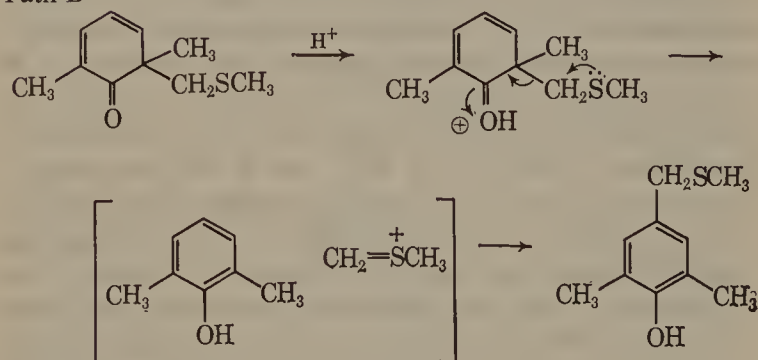
Path A seems generally unlikely since, unlike the case of the *para* Claisen rearrangement, the terminal S–CH₃

(13) These figures are corrected for a 2.15-fold greater hydrogen flame detector response toward 20 relative to 11.
(14) S. J. Rhoads in "Molecular Rearrangements," P. de Mayo, Ed., Interscience Publishers, Inc., New York, N. Y., 1963, p 655.

group of the side chain is essentially unreactive and activation by, *e.g.*, proton abstraction would not be expected under the reaction conditions. We have, however, attempted to rule out the "cartwheel mechanism" of path A through studies with unsymmetrically substituted sulfoxides. To this end we have shown that *o*-cresol reacts quite normally with benzyl methyl sulfoxide[15] and DCC to give the *ortho*-alkylation product **32** in 34% yield. The linkage of the benzyl methyl sulfide grouping to the phenol was shown to be exclusively through the benzylic carbon by nmr spectroscopy, which showed a single benzyl proton and an intact S-methyl group, and by desulfurization to 2-benzyl-6-methylphenol.[1] The preferential formation of this isomer is to be expected since loss of a proton from the intermediate **30** will occur most readily from the benzylic carbon, giving the ylide **31** and thence the *ortho*-alkylated product **32** according to our general mechanism.[1]
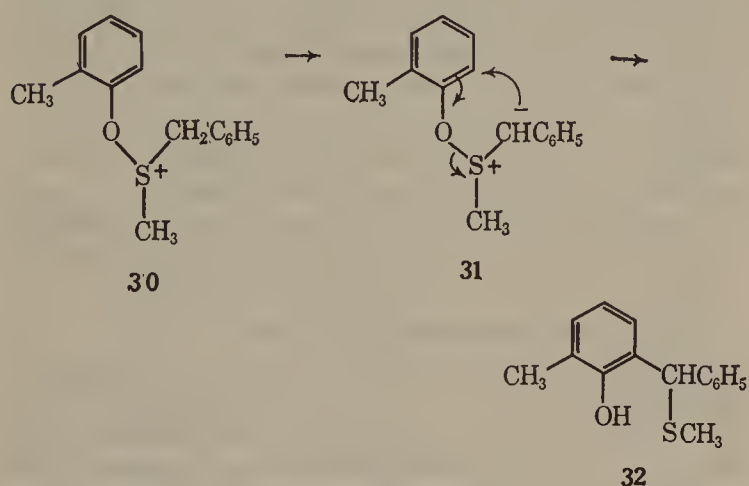
Unfortunately, however, we were unable to isolate any desired cyclohexadienone such as **33** from reaction of benzyl methyl sulfoxide with 2,6-dimethylphenol or durophenol. In both cases substantial amounts of benzaldehyde were formed and, in addition to unreacted phenol, a mixture of inseparable, more polar products was detected by thin layer chromatography. Some material with the characteristic yellow color of the desired dienones was present in this polar fraction but could not be isolated in pure form by preparative thin layer chromatography. From the 2,6-dimethylphenol reaction it was possible to isolate the *para*-alkylation product 2,6-dimethyl-4-(α-thiomethoxybenzyl)phenol (**34**) in 11% yield. The actual yield was undoubtedly much higher, but the separation of **34** from benzaldehyde and 2,6-dimethylphenol was difficult and wasteful. Thin layer chromatography of the crude, extracted reaction mixture showed the presence of **34** without excessive exposure to silicic acid and hence the presumed intermediate dienone must be less stable than those from DMSO (*e.g.*, **13**). As in **32**, the point of attachment of the benzyl methyl sulfide moiety to the phenol in **34** was once again shown to be through the benzylic carbon by nmr spectroscopy. Hence, if we assume that both the *ortho*- and *para*-alkylation products **32** and **34** arise *via* the appropriate dienones (**33a** and **33b**, respectively), a truly concerted intramolecular mechanism such as path A cannot obtain. Definitive proof of this rejection must, however, await the isolation of a pure ketone such as **33b**.

(15) F. G. Bordwell and B. M. Pitt, *J. Am. Chem. Soc.*, 77, 572 (1955).
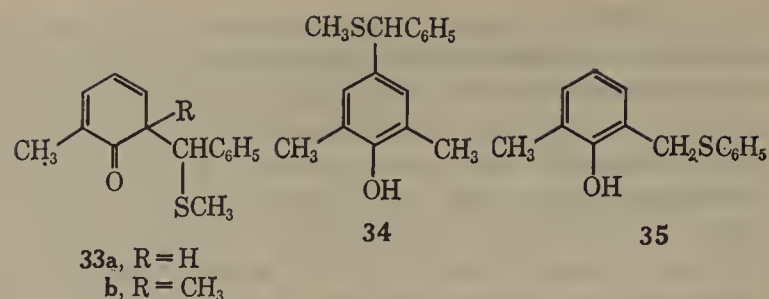
We have also attempted similar studies with two other unsymmetrical sulfoxides which we anticipated could only react in a single way. Thus, while reaction of methyl phenyl sulfoxide and DCC with *o*-cresol was previously shown[1] to give the expected *ortho*-alkylation product **35** in low yield, this sulfoxide failed to give any observable products with 2,6-dimethylphenol.[16] Durophenol also reacted only sluggishly with methyl phenyl sulfoxide and was largely recovered unchanged. One other product was, however, present and was shown to be duroquinone (**37**) which was isolated crystalline in 10% yield. As yet this is the only instance of quinone formation from a monobasic phenol that we have observed,[17] and a likely mechanism involves *para* attack by a second molecule of sulfoxide upon the rather hindered phenoxysulfonium ion **36** followed by ylide formation and intramolecular proton abstraction as in the normal oxidation of alcohols.[3d]
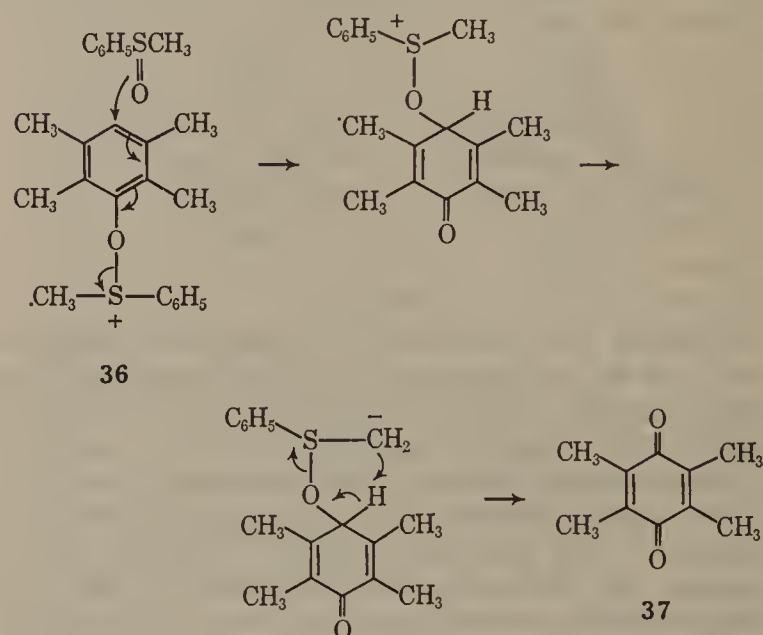
The reaction of *t*-butyl methyl sulfoxide[18] and DCC with *o*-cresol led to the isolation of 2-(*t*-butylthiomethyl)-6-methylphenol (**38**) which gave 2,6-dimethylphenol upon desulfurization. Once again this sulfoxide reacted only poorly with 2,6-dimethylphenol but did give a low yield of 4-(*t*-butylthiomethyl)-2,6-dimethylphenol (**39**), which, upon desulfurization, was converted into crystalline 2,4,6-trimethylphenol. The intermediate cyclohexadienone was not observed. The reaction of *t*-butyl methyl sulfoxide with durophenol did, however, give the very unstable dienone **40** which could not be freed from roughly 10% of an unidentified impurity by chromatography and which decomposed upon attempted distillation. The impure product was identi-

(16) Some slow formation of a dark, insoluble tar did result, but the starting materials were the only ultraviolet absorbing compounds detected in the soluble reaction mixture by thin layer chromatography.
(17) We previously described the conversion of hydroquinone to *p*-benzoquinone upon reaction with DMSO and DCC.[1]
(18) H. G. Henbest, J. A. W. Reid, and C. J. M. Stirling, *J. Chem. Soc.*, 1220 (1964).

fied by its ultraviolet and infrared spectra and particularly by its nmr spectrum which showed the SCH$_2$– group as a typical pair of geminally coupled doublets ($J = 11$ cps) centered at 189 and 162 cps. Attempted acid-catalyzed rearrangement of **40** to the *para*-alkylated phenol led only to the formation of durophenol. The lack of alkylation is perhaps due to facile fragmentation of the methylene-*t*-butylsulfonium ion (**41**) produced by path B into the *t*-butyl carbonium ion and thioformaldehyde.


38

39

40

41
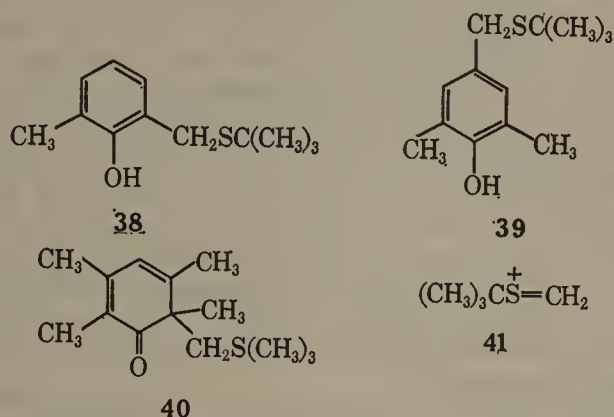
The above experiments generally speak against the formation of *meta*- and *para*-alkylated phenols *via* path A, and we have sought further evidence for the dissociation–recombination mechanism of path B. This was most readily provided by treating a mixture of the ketone **19** from pentamethylphenol and 3 equiv of *o*-cresol with a trace of trifluoroacetic acid. Vapor phase chromatography demonstrated the complete disappearance of **19** within a few minutes with formation of pentamethylphenol and two (thiomethoxymethyl)cresols in a ratio of 1:3. These products were isolated by preparative thin layer chromatography and shown to be 2-methyl-6-(thiomethoxymethyl)phenol (**1**) and 2-methyl-4-(thiomethoxymethyl)phenol (**42**). The minor product **1** was identical with the previously described compound from *o*-cresol, DMSO, and DCC,[1] while the major one was unequivocally identified by its nmr and ultraviolet spectra and by desulfurization to 2,4-dimethylphenol. The latter compound could be distinguished from other isomeric xylenols by vapor phase chromatography and by spectral methods. It is significant that the major point of alkylation is *para* to the phenolic group while the reaction of *o*-cresol with DMSO and DCC leads to exclusively *ortho*-substituted products, thus supporting the intramolecular mechanism previously proposed for the latter reaction.[1]

Thus, while it has been possible to demonstrate facile intermolecular transfer of the thiomethoxymethyl group from the pentamethyl ketone **19** to other nucleophiles, we have also noted a pronounced tendency toward intramolecular alkylation during acid treatment of ketones such as **13** or **18** having unsubstituted 4 positions. These observations are best reconciled by assuming that the methylmethylenesulfonium ion (**29**) and the phenol, which arise by acid-catalyzed dissociation of the dienone according to path B, exist as a rather firmly bound π complex. Such a complex would lead to preferential "intramolecular" recombination but could still give intermolecular alkylation if sufficient amounts of other nucleophiles were present. A similar type of π complex has been proposed by Miller as the transition state in dienone–phenol rearrangements.[19]

(19) B. Miller, *J. Am. Chem. Soc.*, **87**, 5115 (1965).

Phenols containing halogen atoms in the 2 and 6 positions behave somewhat anomolously. Thus, the reaction of pentachlorophenol with DMSO, DCC, and anhydrous phosphoric acid led to the formation of pentachlorophenyl thiomethoxymethyl ether (**43**) which was isolated crystalline in 60% yield. This compound was also obtained in 63% yield through reaction of potassium pentachlorophenolate with chloromethyl methyl sulfide in benzene. The action of acid on **43** regenerated pentachlorophenol. The formation of aryl thiomethoxymethyl ethers was previously shown[1] to be characteristic of only strongly acidic phenols. The reaction with pentachlorophenol (pK = 5.2[20]) is, however, the only case we have studied in which ether formation was the principal reaction. We have previously suggested[1] that ether formation is the consequence either of rearrangement of the phenoxyphosphonium ylide **7** *via* attack by the carbanion on oxygen or of alkylation of the free phenol by the methylmethylenesulfonium species (**29**). On the basis of studies carried out in this laboratory on the reactions of sulfoxides and carbodiimides with a variety of other functional groups, we are now more inclined to accept the dissociation–recombination mechanism.

The reaction of DMSO and DCC with 2,6-dichlorophenol and 2,4,6-trichlorophenol, however, lead to quite different results, the major products being 8-chloro-1,3-benzoxathian (**44**) and 6,8-dichloro-1,3-benzoxathian (**45**), respectively. The formation of these products in yields of 25 and 42% contrast sharply with

42   **43**   **44**   **45**
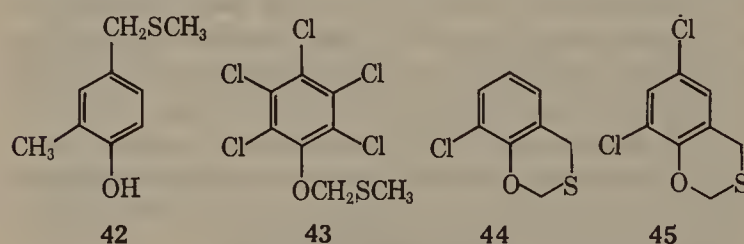
the very low yields (usually about 5%) of benzoxathians resulting from the reactions of most simple phenols.[1] Clearly displacement of chloride ion from one of the *ortho* positions constitutes a significant driving force favoring cyclic products. A possible mechanism would be as shown from **46** → **44**.

46   **47**   **48**

44   **49**
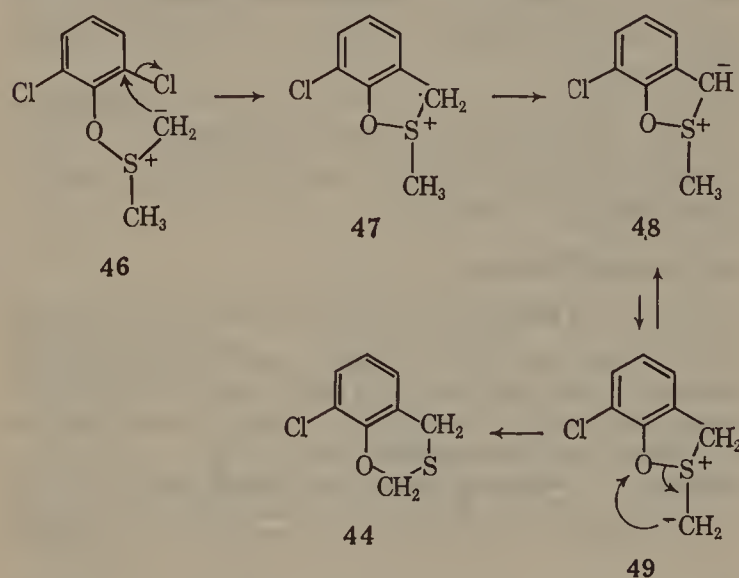
Loss of a proton from the cyclic sulfonium ion **47** would be expected to occur primarily at the benzylic

(20) G. J. Tiessens, *Rec. Trav. Chim.*, **50**, 112 (1931).

carbon, giving ylide **48** which would be relatively inert. The thermodynamically less stable ylide **49** could, however, rearrange with formation of the benzoxathian **44**. Alternatively the ylide **48** could rearrange *via* several noncyclic intermediates, as, *e.g.,* **48 → 44**.
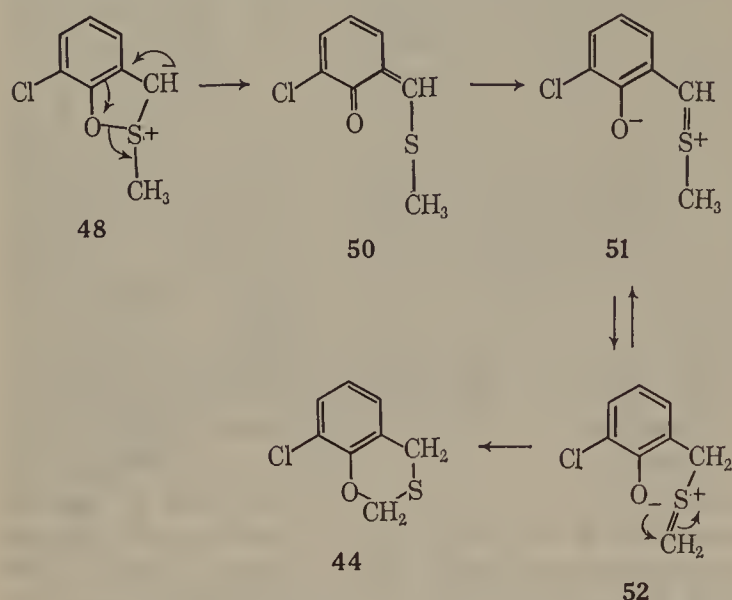
The intervention of the thermodynamically less stable intermediates **49** and **52** in the mechanisms above is very similar to that considered by Wittig, Hauser, and others[21] to occur during the Sommelet rearrangement of benzyltrimethylammonium ions. A decision between these two related pathways cannot be made at this time. An anomalous result accompanied the reaction of *o*-chlorophenol with DMSO and DCC since, instead of the expected unsubstituted 1,3-benzoxathian, the major new product was 8-chloro-1,3-benzoxathian (**44**), identical with the product from 2,6-dichlorophenol. The yield of **44** was only 20%, however, and greater than 50% of the starting material was recovered unchanged. The reason for this relatively high yield of benzoxathian *without* loss of chlorine remains obscure.

Very recently Hayashi and Oda[22] have described the thiomethoxymethylation of several phenols by dimethyl sulfoxide and acetic anhydride and have shown that *para* alkylation of 2,6-dimethylphenol does occur. We, too, have performed some experiments using the DMSO–acetic anhydride mixture and have observed both ring alkylation and O-alkylation, the latter becoming the predominant reaction with more strongly acidic phenols.

In future papers in this series we will describe the reactions of sulfoxides and carbodiimides with a considerable number of other functional groups leading to some unusual products.

Experimental Section

Methods. The general experimental methods used in this work are similar to those described previously.[1] Instrumental analyses were performed by the staff of the Analytical Laboratories of Syntex Research under the direction of Dr. L. Throop. We are particularly grateful to Mr. John Murphy and Dr. Laszlo Tökés for their assistance with nmr and mass spectrometry.

Reactions of 2,6-Dimethylphenol with DMSO and DCC. 2,6-Dimethylphenol (2.44 g, 20 mmoles) was dissolved in a mixture of anhydrous DMSO[23] (20 ml) and benzene (20 ml) containing DCC

(12.36 g, 60 mmoles). A solution of anhydrous orthophosphoric acid in DMSO (2 ml of 5 *M*) was added, and after several minutes an exothermic reaction ensued. After 45 min, thin layer chromatography using benzene showed the starting phenol to be completely absent, having been replaced by a slower moving product. Ether (100 ml) was added and the crystalline dicyclohexylurea (7.2 g) was removed by filtration. The ether solution was then extracted four times with equal volumes of water, dried over sodium sulfate, and evaporated to dryness, leaving 7.40 g of a pale yellow syrup. This was divided into two equal portions which were worked up separately.

a. One portion was chromatographed on a column containing 300 g of Merck silicic acid (0.05–0.12-mm particles) using benzene as eluent. A single, ultraviolet-absorbing product was detected in fractions 60–100 (25 ml each), and these were pooled and evaporated to dryness. The residue immediately crystallized, giving 1.20 g (66%) of 2,6-dimethyl-4-(thiomethoxymethyl)phenol (**11**), mp 40–42°, unchanged on recrystallization from hexane. Analytical and spectral data are given in Tables I and II. A small sample (100 mg) was stirred in methanol (5 ml) with Davidson sponge nickel[6] (1 g) for 1 hr. The nickel was then removed by filtration through Celite and, upon evaporation of the solvent, the residue crystallized. This material was chromatographically homogeneous and, following sublimation, had mp 72–73°. It was indistinguishable from an authentic sample of 2,4,6-trimethylphenol by its infrared and nmr spectra.

b. Examination of the second portion by vapor phase chromatography on a 5-ft column of 5% SE-30 on Gas Chrom Q using a temperature of 130° showed the presence of only a trace of the phenol **11** (retention time 9.8 min) together with major peaks of DCC (retention time 15.7 min) and a more volatile compound (retention time 3.3 min). This material was rapidly[24] chromatographed on four 1 m × 20 cm preparative silica plates coated with a 1.3-mm layer of Merck silica HF.[7] The yellowish band with an R_f of 0.2–0.3 was removed, eluted with methylene chloride, and evaporated to dryness, leaving 1.60 g of a pale yellow oil. Vapor phase chromatography of this material showed the presence of about 20% of the rearranged phenol **11** which was removed by repeated extraction of a solution of the mixture in ether with 0.25 *N* sodium hydroxide. The ether solution was then washed with water, dried over sodium sulfate, and evaporated, leaving 1.20 g (66%) of 2,6-dimethyl-6-(thiomethoxymethyl)cyclohexa-2,4-dien-1-one (**13**) which was homogeneous by thin layer and vapor phase chromatography. The product could be distilled as a clear yellow oil in a "Kugelrohr" short-path apparatus[25] with a bath temperature of 60° at 10⁻⁴ mm. Immediately following distillation **13** showed a single carbonyl band at 1650 cm⁻¹ (see Tables I and II for other analytical and spectral data). Upon storage of 300 mg of pure **13** at room temperature for several days a considerable amount of crystalline material separated. The mixture was diluted with pentane and filtered, leaving 120 mg (40%) of white crystals, mp 116–125°, which behaved identically with **13** on vapor phase chromatography. Repeated crystallization from ethanol gave a pure isomer of the dimer **14**, mp 130–131°. This material showed carbonyl bands at 1675 and 1715 cm⁻¹. Mass spectrometry showed a molecular ion (relative intensity 56%) at *m/e* 364 and other significant features which are discussed in the text.

Addition of trifluoroacetic acid (10 μl) to a solution of **13** (100 mg) in methylene chloride led to the immediate disappearance of the yellow color and complete rearrangement to the phenol **11** which was identified by vapor phase chromatography and by crystallization of the evaporated reaction mixture.

Similar reactions between 2,6-dimethylphenol, DMSO, and DCC in the presence of 10 equiv of furan, anisole, or 1,3-dimethoxybenzene led to identical products, as judged by vapor phase chromatography. No evidence of alkylation of the additives could be detected.

Reaction of 2,4,6-Trimethylphenol with DMSO and DCC. A reaction between 2,4,6-trimethylphenol (2.72 g, 20 mmoles) and DCC (12.36 g, 60 mmoles) in DMSO (20 ml) and benzene (20 ml) containing 10 mmoles of anhydrous orthophosphoric acid was worked up after 2 hr exactly as described above with 2,6-dimethylphenol. The crude, extracted product (6.6 g) was divided into two equal portions and handled separately as follows.

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(21) (a) G. Wittig, R. Mangold, and G. Felletschin, *Ann.,* **560,** 117 (1948); (b) K. P. Klein and C. R. Hauser, *J. Org. Chem.,* **31,** 4276 (1966); (c) H. E. Zimmerman, ref 14, p 378.

(22) Y. Hayashi and R. Oda, *J. Org. Chem.,* **32,** 457 (1967).

(23) Dried by distillation *in vacuo* and storage over Linde Molecular Sieve Type 4A.

(24) The entire procedure, including application to the plates, development, and elution of the product, was completed in less than 2 hr.

(25) R. Graeve and G. H. Wahl, *J. Chem. Educ.,* **41,** 279 (1964).

a. One portion was rapidly chromatographed on four 1 m × 20 cm preparative silica plates using benzene, and the resulting major band was eluted with methylene chloride, leaving 1.83 g (93%) of 2,4,6-trimethyl-6-(thiomethoxymethyl)cyclohexa-2,4-dien-1-one (15) as a clear yellow oil that was homogeneous by vapor phase chromatography (retention time 4.9 min at 130° on a 5-ft SE-30 column). This material could be distilled in a short-path apparatus (65° (10⁻⁴ mm)) with negligible loss and showed ν_{max} 1645 cm⁻¹. Other analytical and spectral data are in Tables I and II. Addition of trifluoroacetic acid (5 μl) to a solution of 15 (10 mg) in methylene chloride (0.05 ml) led to the formation of 90–95% of the isomeric phenol 12 and 5–10% of 2,4,6-trimethylphenol as determined by vapor phase chromatography.

b. The second portion was chromatographed on a column containing 300 g of Merck silicic acid using benzene and collecting 20-ml fractions. Fractions 69–102 contained 0.35 g (18%) of 2,4,6-trimethyl-3-(thiomethoxymethyl)phenol (12) which crystallized spontaneously and could be recrystallized from hexane, mp 85–86° (see Tables I and II). Fractions 103–240 contained 1.20 g of a yellow oil that was shown by vapor phase chromatography to be a mixture of 30% 12 and 70% of the ketone 15. In this case the phenol could not be extracted with alkali.

Desulfurization of 12 with sponge nickel in methanol at room temperature led to complete conversion to 2,3,4,6-tetramethylphenol, mp 77–78°, which was identical with an authentic sample.

Reaction of Durophenol with DMSO and DCC. a. Freshly crystallized (methanol) durophenol (1.50 g, 10 mmoles) was allowed to react at room temperature for 2 hr with DCC (6.18 g, 30 mmoles) and anhydrous phosphoric acid (5 mmoles) in a mixture of DMSO (10 ml) and benzene (10 ml). The reaction was worked up as above, giving 3.70 g of a yellow oil that was shown by vapor phase chromatography on a 5-ft column of 10% NPGS on Gas Chrom Q at 145° to contain essentially nothing but a mixture of DCC (5.7 min) and the desired ketone (4.5 min). This material was chromatographed on four 1 m × 20 cm preparative silica plates using benzene, elution of the ultraviolet-absorbing band giving 1.80 g (86%) of 2,3,5,6-tetramethyl-6-(thiomethoxymethyl)cyclohexa-2,4-dien-1-one (18) as a chromatographically homogeneous yellow oil that was distilled in a short-path apparatus (90° bath at 10⁻³ mm) with 1.60-g recovery; $\nu_{max}^{CHCl_3}$ 1635 cm⁻¹ (see Tables I and II for other data).

Desulfurization of 18. The thiomethoxymethyl ketone 18 (420 mg, 2 mmoles) was dissolved in methanol (20 ml) and Davidson sponge nickel (4–5 g) was added. After stirring at room temperature for 2 hr thin layer chromatography with benzene showed the disappearance of the starting material accompanied by the appearance of two ultraviolet-absorbing and one nonultraviolet-absorbing products. The mixture was filtered through Celite and the filtrate was chromatographed on a 1-m-long preparative silica plate using benzene–chloroform (7:2), the two ultraviolet-absorbing bands then being eluted with acetone. The faster band (100 mg) was distilled in a micro short-path apparatus at 40° (10⁻⁴ mm), giving 90 mg of 2,3,5,6,6-pentamethylcyclohex-2-en-1-one (21) as a colorless oil, λ_{max}^{MeOH} 243 mμ (ε 9100) ν_{max} 1655 cm⁻¹. The nmr spectrum showed two vinyl methyl groups as singlets at 113 and 106 cps, two quaternary methyl groups as singlets at 54 and 66 cps, one secondary methyl group as a multiplet at 50–75 cps, and two allylic protons at 120–140 cps.

Anal. Calcd for C₁₁H₁₈O: C, 77.86; H, 11.76; O, 10.37. Found: C, 78.33; H, 11.26; O, 10.20.

The slower band (130 mg) was distilled *in vacuo* at 60° (10⁻⁴ mm), giving 2,3,5,6-tetramethyl-6-(thiomethoxymethyl)cyclohex-2-en-1-one (23), λ_{max}^{MeOH} 243 mμ (ε 10,800); ν_{max} 1650 cm⁻¹. The nmr spectrum in deuteriochloroform clearly confirmed structure 23 and showed a –SCH₃ group as a singlet at 115 cps, the –CH₂S as a pair of geminally coupled doublets (J = 13 cps) at 151 and 193 cps, two aliphatic methyl groups as a broad singlet at 57 cps, two vinylic methyl groups as singlets at 107 and 127 cps, and two allylic protons as a broad singlet at 138 cps.

2,3,5,6-Tetramethyl-4-(thiomethoxymethyl)phenol (20). 2,3,5,6-Tetramethyl-6-(thiomethoxymethyl)cyclohexa-2,4-dien-1-one (18, 210 mg, 1 mmole) was dissolved in methylene chloride, and trifluoroacetic acid (25 μl) was added. Within 10 min the yellow color had disappeared and a mass of white crystals had separated. The solvent was evaporated *in vacuo* and the residue was crystallized from methanol, giving 195 mg (93%) of 2,3,5,6-tetramethyl-4-(thiomethoxymethyl)phenol (20), mp 144–145° (see Tables I and II for analytical and spectral data).

Desulfurization of 20 with Davidson sponge nickel in methanol led to quantitative conversion to pentamethylphenol, mp 129–130°,

following sublimation *in vacuo* at 100°. This product had an identical infrared spectrum with that of an authentic sample.

2,3,4,5,6-Pentamethyl-6-(thiomethoxymethyl)cyclohexa-2,4-dien-1-one (19). Commercial pentamethylphenol²⁶ was purified by repeated treatment with activated charcoal in hot methanol and then crystallized twice from methanol to give pale yellow needles, mp 129–130°. This material (1.64 g, 10 mmoles) was dissolved in a mixture of DMSO (20 ml) and benzene (20 ml) and allowed to react with DCC (6.18 g, 30 mmoles) and anhydrous orthophosphoric acid (5 mmoles). After 1 hr the reaction was worked up as described for 2,6-dimethylphenol and chromatographed on six 1-m-long preparative silica plates using benzene–chloroform (6:1). The resulting yellow band was eluted with methylene chloride and the extracts were evaporated, leaving 0.95 g (85%) of 19 as a chromatographically homogeneous clear yellow oil which was distilled in a short-path apparatus at 80° (10⁻⁴ mm); $\nu_{max}^{CHCl_3}$ 1630 and 1650 cm⁻¹. Other analytical and spectral data are in Tables I and II.

Desulfurization of 440 mg (2 mmoles) of 19 in methanol (20 ml) containing 4–5 g of Davidson sponge nickel was carried out at room temperature for 4 hr. Following filtration through Celite the filtrate was chromatographed on 2-m-long preparative silica plates using two consecutive developments with benzene–chloroform (7:2). The main ultraviolet-absorbing band was eluted with methylene chloride and evaporated, leaving 150 mg (42%) of 2,3,4,5,6,6-hexamethylcyclohex-2-en-1-one (22) which was distilled in a micro short-path apparatus at 60° (10⁻⁴ mm); λ_{max}^{MeOH} 246 mμ (ε 10,700); ν_{max} 1660 cm⁻¹. The nmr spectrum in deuteriochloroform showed two vinylic methyl groups as rough singlets at 107 and 114 cps, a secondary methyl group as a doublet (J = 7 cps) at 52 cps, and three other methyl groups as superimposed signals at 65–73 cps.

Anal. Calcd for C₁₂H₂₀O: C, 79.94; H, 11.18. Found: C, 79.75; H, 11.00.

Reaction of 2,3,4,6-Tetramethylphenol with DMSO and DCC. 2,3,4,6-Tetramethylphenol (1.50 g, 10 mmoles) was allowed to react overnight at room temperature with DCC (6.18 g) and anhydrous orthophosphoric acid (5 mmoles) in DMSO (15 ml) and benzene (5 ml). The reaction was worked up as above for 2,6-dimethylphenol, giving 4.0 g of a yellow oil which was chromatographed on four 1-m-long preparative silica plates using benzene–chloroform (4:1). The single yellow band was eluted with methylene chloride, giving 2.0 g (95%) of a yellow oil that was distilled in a short-path apparatus at 80° (10⁻³ mm). This product appeared homogeneous by vapor phase and thin layer chromatography but, from its nmr spectrum, was clearly a mixture of roughly 60% 2,3,4,6-tetramethyl-6-(thiomethoxymethyl)cyclohexa-2,4-dien-1-one (25) and 40% of the 2,4,5,6-tetramethyl isomer 26. The spectrum of the mixture showed a quaternary methyl group as a singlet at 69 cps, a –SCH₃ singlet at 121 cps, and three vinylic methyl singlets at 112, 113, and 117 cps. The single vinyl proton of 25 was a broadened singlet at 358 cps, while that of 26 appeared at 405 cps. The S–CH₂ groups appeared as overlapping quartets at 151–194 cps, all showing geminal coupling of 12 cps; $\nu_{max}^{CHCl_3}$ 1645 cm⁻¹ (other analytical and spectral data are in Tables I and II).

2,3,4,6-Tetramethyl-5-(thiomethoxymethyl)phenol (27). The mixed ketones 25 and 26 (420 mg, 2 mmoles) were dissolved in methylene chloride (8 ml), and trifluoroacetic acid (0.1 ml) was added. After 1 hr the colorless solution was evaporated to dryness and chromatographed on a 1-m-long preparative silica plate using benzene. Two ultraviolet-absorbing bands resulted and were eluted with methylene chloride. The material from the faster band (130 mg) proved to be 2,3,4,6-tetramethylphenol while that from the slower band (150 mg, 60% from 25) was recrystallized from cyclohexane, giving 2,3,4,6-tetramethyl-5-(thiomethoxymethyl)phenol (27), mp 97–98° (see Tables I and II). Desulfurization of 25 mg of 27 gave crystalline pentamethylphenol, identical with an authentic sample.

Benzyl Methyl Sulfoxide. Benzyl methyl sulfide²⁷ (35 g) was dissolved in acetic acid (100 ml), and 30% hydrogen peroxide (25 ml) was added slowly over 30 min with ice cooling. The mixture was allowed to stand overnight and then added to a solution of sodium hydroxide (80 g) in water (500 ml). Extraction of the clear solution with ether according to Bordwell and Pitt¹⁵ failed to extract the sulfoxide, but extraction with methylene chloride gave 36 g of a colorless oil. Upon addition of ether the entire mass crystal-

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(26) Aldrich Chemical Co., Milwaukee, Wis.

(27) Columbia Organic Chemicals Co., Columbia, S. C.

lized, giving 29 g of colorless benzyl methyl sulfoxide, mp 55–56°.[28]

2-Methyl-6-(α-thiomethoxybenzyl)phenol (32). o-Cresol (1.1 g, 10 mmoles), benzyl methyl sulfoxide (3.1 g, 20 mmoles), DCC (6.18 g, 30 mmoles), and anhydrous phosphoric acid (5 mmoles) were dissolved in dry ether (20 ml) and allowed to stand overnight. A gummy precipitate separated rapidly.[29] A solution of oxalic acid (3.78 g, 30 mmoles) in methanol was added, and after 30 min the mixture was diluted with water (100 ml) and ether (100 ml) and filtered. The ether layer was extracted with aqueous sodium bicarbonate, then twice with water, and dried over sodium sulfate. Thin layer chromatography using benzene showed the presence of considerable unreacted o-cresol, an intense spot of benzaldehyde, two minor by-products near the solvent front, and a principal product with R_f 0.7. The mixture was chromatographed on a column containing 150 g of Merck silicic acid using benzene, giving 828 mg (34%) of 2-methyl-6-(α-thiomethoxybenzyl)phenol (32) as a chromatographically homogeneous oil that could be distilled in a short-path apparatus at 100° (10^{-4} mm); λ_{max}^{MeOH} 277 mμ (ε 2400); $\lambda_{max}^{OH^-}$ 283 mμ (ε 2100), 303 mμ (ε 2300). The nmr spectrum showed three-proton singlets at 122 (SCH$_3$) and 137 cps (ArCH$_3$), a one-proton singlet at 315 cps (Ar$_2$CHS), eight aromatic protons as a multiplet at 400–460 cps, and a phenolic proton at 422 cps.

Anal. Calcd for C$_{15}$H$_{16}$OS: C, 73.75; H, 6.60; S, 13.10. Found: C, 73.94; H, 6.71; S, 13.42.

Desulfurization with sponge nickel catalyst in refluxing methanol for 1 hr gave 2-benzyl-6-methylphenol identical with an authentic sample.[1]

2,6-Dimethyl-4-(α-thiomethoxybenzyl)phenol (34). 2,6-Dimethylphenol (610 mg, 5 mmoles), benzyl methyl sulfoxide (1.54 g, 10 mmoles), and DCC (3.09 g, 15 mmoles) were dissolved in anhydrous dimethylformamide (5 ml), and a solution of anhydrous orthophosphoric acid in ether (1.0 ml of 2.5 M) was added. An exothermic reaction ensued, and the mixture was allowed to stand overnight. Ether (100 ml) was added and, after filtration of dicyclohexylurea, the solution was extracted four times with water and then dried over sodium sulfate. Evaporation left 3.4 g of a yellow oil that was chromatographed on six 1-m-long preparative silica plates using benzene. The desired product ran immediately behind unreacted 2,6-dimethylphenol, from which it was largely resolved. A slightly faster band containing 100 mg of benzaldehyde (identified by vapor phase chromatography and formation of a 2,4-dinitrophenylhydrazone) and a slower moving yellowish band containing at least three different products were also present. The desired band was eluted with methylene chloride, giving 0.50 g of product still contaminated with some starting material and benzaldehyde. This was rechromatographed on two preparative silica plates using three consecutive developments with benzene–carbon tetrachloride (9:1) which gave 142 mg (11%) of chromatographically pure 2,6-dimethyl-4-(α-thiomethoxybenzyl)phenol (34) as an oil that was distilled in a short-path apparatus at 100° (10^{-4} mm); λ_{max}^{MeOH} 233 mμ (shoulder) (ε 8000), 278 mμ (ε 1600). The nmr spectrum showed a three-proton singlet at 117 cps (SCH$_3$), a six-proton singlet at 130 cps (2 ArCH$_3$), and a one-proton singlet at 298 cps (Ar$_2$CHS), as well as a phenolic proton and seven aromatic protons between 410 and 460 cps.

Anal. Calcd for C$_{16}$H$_{18}$OS: C, 74.39; H, 7.02; S, 12.38. Found: C, 74.64; H, 7.20; S, 12.46.

Reaction of Durophenol with Methyl Phenyl Sulfoxide. Durophenol (1.5 g, 10 mmoles) was dissolved in ether (20 ml) containing methyl phenyl sulfoxide[30] (2.8 g, 20 mmoles), DCC (6.18 g, 30 mmoles), and anhydrous phosphoric acid (5 mmoles). Ether (100 ml) was added and, after filtration of dicyclohexylurea, the solution was extracted with water and dried. Chromatography of the residue on a column containing 150 g of silicic acid with benzene gave a mixture (1.2 g) of unreacted durophenol and a more polar product, rechromatography of which gave 163 mg (10%) of 1,4-duroquinone as yellow needles, mp 112–115° after crystallization from hexane. This product had an identical melting point and infrared spectrum with that of an authentic sample of duroquinone.

2-(t-Butylthiomethyl)-6-methylphenol (38). o-Cresol (1.1 g, 10 mmoles) was allowed to react overnight in ether (20 ml) containing t-butyl methyl sulfoxide[18] (3.0 ml, 25 mmoles), DCC (6.18 g, 30 mmoles), and anhydrous phosphoric acid (5 mmoles). Follow-

ing filtration and extraction with water the residue was chromatographed on a column containing 100 g of silicic acid. A fast-moving, ultraviolet-absorbing band was eluted giving 565 mg (27%) of chromatographically pure 38 which was distilled in a short-path apparatus at 80° (10^{-3} mm); λ_{max}^{MeOH} 277 mμ (ε 1800); $\lambda_{max}^{OH^-}$ 297 mμ (ε 1100) and 282 mμ (ε 2000). The nmr spectrum showed the t-butyl group as a nine-proton singlet at 81 cps, a three-proton singlet (ArCH$_3$) at 135 cps, a two-proton singlet (ArCH$_2$S) at 231 cps, and three aromatic protons and a phenolic proton between 400 and 440 cps.

Anal. Calcd for C$_{12}$H$_{18}$OS: C, 68.54; H, 8.63; S, 15.22. Found: C, 68.43; H, 8.51; S, 15.26.

4-(t-Butylthiomethyl)-2,6-dimethylphenol (39). 2,6-Dimethylphenol (3.05 g, 25 moles) was allowed to react overnight in benzene (20 ml) with t-butyl methyl sulfoxide (10 ml), DCC (15 g), and anhydrous phosphoric acid (1.2 g). Thin layer chromatography detected the presence of much unreacted 2,6-dimethylphenol together with a slightly slower moving product and a second trace compound. The reaction was worked up in the usual way and gave, after chromatography twice on columns of silicic acid with benzene and distillation at 100° (10^{-3} mm), 100 mg (2%) of pure 39 as an oil; λ_{max}^{MeOH} 277 mμ (ε 1700). The nmr spectrum showed the t-butyl group as a nine-proton singlet at 81 cps, a six-proton singlet (2 ArCH$_3$) at 133 cps, a two-proton singlet (ArCH$_2$S) at 220 cps, a one-proton singlet (phenol) at 274 cps, and two aromatic protons as a singlet at 418 cps.

Anal. Calcd for C$_{13}$H$_{20}$OS: C, 69.61; H, 8.99; S, 14.28. Found: C, 69.41; H, 8.82; S, 14.01.

Desulfurization of this product (25 mg) with Davidson sponge nickel in boiling methanol gave a single crystalline product, mp 70–71°, which was physically and spectrally identical with 2,4,6-trimethylphenol.

6-(t-Butylthiomethyl)-2,3,5,6-tetramethylcyclohexa-2,4-dien-1-one (40). Durophenol (2.8 g, 25 mmoles) was allowed to react overnight in benzene (25 ml) with DCC (15.5 g, 75 mmoles), t-butyl methyl sulfoxide (10 ml), and dichloroacetic acid (1.03 ml, 12.5 mmoles). The reaction was worked up in the usual way and chromatographed on a column containing 250 g of silicic acid using benzene.[31] A yellow band (2.0 g) was obtained and rechromatographed on a second column, but completely homogeneous material was not obtained. The yellow oil decomposed to a black tar containing durophenol upon attempted short-path distillation and appeared to be unstable on storage at room temperature. Its identification as 40 was based on its ultraviolet (λ_{max}^{MeOH} 323 mμ), infrared (ν_{max} 1650, 1680 cm^{-1}), and nmr spectra (t-butyl and quaternary methyl groups as a singlet at 75 cps, the –CH$_2$S– group as a pair of geminally coupled doublets ($J = 11$ cps) at 162 and 189 cps, a single vinyl proton as a singlet at 365 cps, and the vinyl methyl groups plus an unidentified impurity corresponding to roughly three protons as a multiplet at 105–135 cps). Treatment with one drop of concentrated hydrochloric acid in methanol led to complete conversion to durophenol.

Pentachlorophenyl Thiomethoxymethyl Ether (43). a. Pentachlorophenol (6.6 g, 25 mmoles) was allowed to react exothermically in benzene (20 ml) with DCC (15.5 g, 75 mmoles), DMSO (15 ml), and anhydrous phosphoric acid (12.5 mmoles). After standing overnight the mixture was diluted with ether (100 ml), filtered, and extracted four times with water. It was then extracted several times with 0.5 N sodium hydroxide and the nonphenolic fraction was chromatographed on a column containing 150 g of silicic acid with benzene–hexane (1:1). A single ultraviolet-absorbing product (4.9 g, 60%) was obtained and crystallized from methanol, giving 43 as white needles, mp 87–88°; λ_{max}^{MeOH} 214 (ε 85,500), 292 (520), and 300 mμ (550). The nmr spectrum shows only a three-proton singlet (SCH$_3$) at 143 cps and a two-proton singlet (OCH$_2$S) at 315 cps.

b. Pentachlorophenol (2.64 g, 10 mmoles) and potassium hydroxide (0.56 g, 10 mmoles) were dissolved in methanol (20 ml) and the solution was evaporated to dryness, leaving the crystalline potassium salt which was dried in vacuo. It was then suspended in benzene (50 ml) together with chloromethyl methyl sulfide (10 ml) and refluxed for 1 hr. Ether (50 ml) was added and the solution was extracted three times with 0.5 N sodium hydroxide. The ether solution was dried, evaporated, and chromatographed on a column containing 80 g of silicic acid with benzene–hexane (1:1). The major product was evaporated and crystallized from methanol, giving 2.06 g (63%) of 43 identical with that above.

(28) A. Cerniani, G. Modena, and P. E. Todesco, *Gazz. Chim. Ital.*, 90, 3 (1960), report mp 57–58° by a different route.

(29) We later showed that only dicyclohexylurea separated if dimethylformamide was used as the solvent. The yield of 32 was similar.

(30) C. C. Price and J. J. Hydock, *J. Am. Chem. Soc.*, 74, 1943 (1952).

(31) When the crude, extracted reaction mixture was dissolved in ether, 1.0 g of N-dichloroacetyl-N,N'-dicyclohexylurea, mp 145–147°, crystallized out.

6,8-Dichloro-1,3-benzoxathian (45). 2,4,6-Trichlorophenol (4.92 g, 25 mmoles) was allowed to react overnight with DCC (15.5 g, 75 mmoles) and anhydrous phosphoric acid (12.5 mmoles) in a mixture of benzene (25 ml) and DMSO (15 ml). Following removal of dicyclohexylurea and extraction with water, the phenolic and nonphenolic components were separated by extraction with 0.5 N sodium hydroxide. The nonphenolic fraction contained one major product that was isolated by chromatography on a column of silicic acid using benzene–hexane (1:1). On evaporation of the solvent the product crystallized spontaneously and, after recrystallization from hexane, gave 2.3 g (42%) of **45**, mp 126–127°; λ_{max}^{MeOH} 231 (ϵ 10,600), 285 (2900), and 295 mμ (2900). The nmr spectrum showed a two-proton singlet (ArCH$_2$S) at 231 cps, a two-proton singlet (OCH$_2$S) at 319 cps, and two aromatic protons as doublets ($J = 2.5$ cps) at 417 and 436 cps.

Anal. Calcd for C$_8$H$_6$OSCl$_2$: C, 43.48; H, 2.74; S, 14.51; Cl, 32.16. Found: C, 43.64; H, 2.89; S, 14.31; Cl, 32.03.

8-Chloro-1,3-benzoxathian (44). a. 2,6-Dichlorophenol (4.1 g, 25 mmoles) and DCC (15.5 g, 75 mmoles) were allowed to react overnight in benzene (20 ml) and DMSO (15 ml) containing anhydrous phosphoric acid (12.5 mmoles). After removal of dicyclohexylurea and extraction of the DMSO the resulting ether solution was extracted three times with 0.5 N sodium hydroxide, giving primarily unreacted starting phenol. The nonphenolic fraction was chromatographed on a column of silicic acid using benzene–hexane (1:1), giving one principal ultraviolet-absorbing product. This was then distilled in a short-path apparatus at 50° (10⁻³ mm), giving 1.17 g (25%) of 8-chloro-1,3-benzoxathian; λ_{max}^{MeOH} 277 mμ (ϵ 1950) and 285 mμ (ϵ 1850). The nmr spectrum showed two-proton singlets at 231 (ArCH$_2$S) and 318 cps (SCH$_2$O) and three aromatic protons between 405 and 440 cps.

Anal. Calcd for C$_8$H$_7$OSCl: C, 51.46; H, 3.78; S, 17.19; Cl, 19.02. Found: C, 51.17; H, 3.89; S, 17.04; Cl, 18.74.

b. o-Chlorophenol (2.06 ml, 20 mmoles) was allowed to react for 4 hr with DCC (12.4 g, 60 mmoles) and anhydrous phosphoric acid (10 mmoles) in a mixture of benzene (10 ml) and DMSO (20 ml). The mixture was worked up as above, giving 1.26 g (50%) of almost pure unreacted o-chlorophenol in the phenolic fraction and 0.75 g (20%) of **44** after chromatography of the nonphenolic portion. The material was indistinguishable from that obtained above.

Intramolecularity of Rearrangement of Dienones. Vapor phase chromatography of an equimolar mixture of 2,6-dimethyl-4-(thiomethoxymethyl)phenol (**11**) and 2,3,4,6-tetramethyl-4-(thiomethoxymethyl)phenol (**20**) on a 5-ft column of 10% neopentyl glycol succinate on Gas Chrom Q[32] at 160° consistently showed that the integrated detector response toward **20** was 2.15 times that toward **11**.[33]

a. A mixture of the dienone **18** (21 mg, 0.1 mmole) and 2,6-dimethylphenol (61 mg, 0.5 mmole) was dissolved in methylene chloride (0.25 ml), and trifluoroacetic acid (10 μl) was added. Almost immediately the yellow color disappeared, and after 20 min the mixture was directly examined by vapor phase chromatography as above. The integrated intensities of the peaks corre-

sponding to **20** and **11** were in a ratio of 4.40:1, which, after correction for the differences of detector response, indicated the formation of 67% **20** and 33% **11**. The only other peaks present were those of excess 2,6-dimethylphenol and durophenol.

b. The 2,6-dimethyldienone **13** (18 mg, 0.1 mmole) and durophenol (75 mg, 0.5 mmole) were dissolved in methylene chloride (0.25 ml), and trifluoroacetic acid (10 μl) was added. Disappearance of the yellow color was almost instantaneous, and after 20 min vapor phase chromatography showed the products to be **11** and **20** in a ratio of 3.0:1.

Alkylation of o-Cresol by the Pentamethyl Ketone 19. 2,3,4,5,6-Pentamethyl-6-(thiomethoxymethyl)cyclohexa-2,4-dien-1-one (**19**, 224 mg, 1 mmole) and o-cresol (324 mg, 3 mmoles) were dissolved in methylene chloride (0.5 ml), and trifluoroacetic acid (25 μl) was added. After 10 min vapor phase chromatography (5-ft NPGS column at 150°) showed the complete absence of **19** and formation of two products with retention times of 15.7 and 3.1 min with integrated intensities in a ratio of 3.0:1. The latter peak was identical with that of authentic **1**. The only other significant products were excess o-cresol (1.2 min) and pentamethylphenol (7.7 min). The entire mixture was then evaporated to dryness and chromatographed on 2-m-long preparative silica plates using benzene as eluent. Four ultraviolet-absorbing bands were obtained and were eluted with methylene chloride. The fastest band gave 33 mg (20%) of a homogeneous oil that was identical in all respects with an authentic sample of **1**. The second and third bands contained respectively 140 mg of crystalline pentamethylphenol and 133 mg of o-cresol, while the slowest band gave 76 mg (45%) of a chromatographically homogeneous oil identified as 2-methyl-4-(thiomethoxymethyl)phenol (**42**) which was distilled in a short-path apparatus at 60° (10⁻³ mm); λ_{max}^{MeOH} 280 mμ (ϵ 1850) and 229 mμ (ϵ 7850); λ_{max}^{OH-} 289 mμ (ϵ 2350) and 252 mμ (ϵ 8200).[34] The 100-Mc nmr spectrum showed the thiomethoxymethyl group as two singlets at δ 2.01 (SCH$_3$) and 3.59 (ArCH$_2$S), and the aromatic methyl group as a singlet at δ 2.24. The aromatic protons appeared as a doublet ($J = 8$ cps) at δ 6.68 (C-6) and a quartet ($J_{ortho} = 8$ cps, $J_{meta} = 3$ cps) centered at δ 6.98 (C-5). The C-3 proton appeared as a broad singlet at δ 7.04 overlapping the low-field half of the C-5 quartet.[35]

Anal. Calcd for C$_9$H$_{12}$OS: C, 64.27; H, 7.19; S, 19.02. Found: C, 64.17; H, 7.26; S, 18.94.

Desulfurization of a sample of **42** with Davidson sponge nickel in methanol at room temperature for 30 min gave a single spot on thin layer chromatograms with an R_f identical with that of 2,4-dimethylphenol. This identity was confirmed by vapor phase chromatography on a 5-ft column of 10% NPGS on Gas Chrom Q[32] at 105° which clearly separated the desulfurization product from 2,6- and 2,3-dimethylphenols. It ran identically with 2,4- and 2,5-dimethylphenols, but the latter structure could be ruled out by the nmr spectrum of **42**.

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(32) Applied Science Laboratories, State College, Pa.

(33) 2,6-Dimethylphenol (retention time 1.4 min), durophenol (2.6 min), and the ketone **18** (2.3 min) were all clearly separated from substituting phenols **11** (11.2 min) and **20** (35.7 min) on this column.

(34) These spectra are reasonably consistent with those of 2,4-dimethylphenol but differ markedly from those of the isomeric xylenols. See "Organic Electronic Spectral Data," Vol. IV, J. P. Phillips and F. C. Nachod, Ed., Interscience Publishers, Inc., New York, N. Y., 1959, p 179.

(35) This aromatic pattern closely resembles that of 2,4-dimethylphenol and is not consistent with that from 2,3-, 2,5-, or 2,6-dimethylphenols.

Stable Carbonium Ions. XLVI.[1] Protonated Acetyl- and Benzoylpyridinium Ions

George A. Olah and Mihai Calin[2]

Contribution from the Department of Chemistry, Case Western Reserve University, Cleveland, Ohio 44106. Received April 21, 1967

Abstract: Protonated 2-, 3-, and 4-acetyl- and -benzoylpyridinium ions were investigated with nmr spectroscopy at −60° in FSO₃H–SbF₅–SO₂ solution. Analysis of the spectra allowed the elucidation of the structure of protonated acetyl- and benzoylpyridinium ions.

In searching for model compounds for organic dications, we felt it of interest to carry out an investigation of the protonated isomeric (2-, 3-, and 4-) acetyl- and benzoylpyridinium ions. These model compounds were considered of added interest because it was expected that the isomeric ions would yield some information on the proximity effect of the two positive charges. Whereas nmr spectral studies of pyridinium ions and alkyl-substituted pyridinium ions are known,[3] no similar studies on acetyl- and benzoylpyridinium ions are available. Thus we included these ions in our investigation, even more so because they helped in the structural assignments of the diprotonated species.

Results and Discussion

The isomeric (2-, 3-, and 4-substituted) acetyl- and benzoylpyridines were commercially available and were purified before use. The acetyl- and benzoylpyridinium ions were investigated as the hydrochloride salts in sulfur dioxide solution at −60°. Investigation of protonated acetyl- and benzoylpyridinium ions was carred out at −60° in sulfur dioxide solution using the strong acid system HSO₃F–SbF₅ as protonating agent.
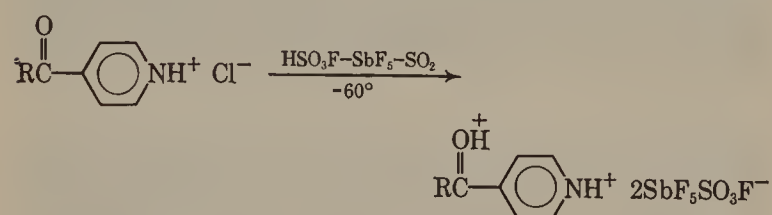
The assignment of pyridine and pyridinium ring hydrogens was made according to the analyzed spectra of 2-acetylpyridine[4] and 3-acetylpyridine.[5] The chemical shifts are approximate since the spectra of the pyridinium ions were not fully analyzed and the assignments were made on the basis of a first-order interpretation. We assume that the error introduced by this method of analysis is within 0.05 ppm, which is sufficient for our purpose. The isomeric (2-, 3-, or 4-) acetyl- and benzoylpyridinium hydrochlorides give well-resolved nmr spectra in sulfur dioxide at −60°.

The chemical shifts summarized in Tables I and II show a large low-field shift compared with those of the free bases. It is, however, important to be aware that a solvent effect may very likely contribute to some extent to the low-field shifts. The proton on nitrogen is observed in sulfur dioxide solution at −60° and appears at −14.5 to −14.8 ppm and −14.7 to −15.1 ppm for acetyl- and benzoylpyridinium, respectively. The appearance of the proton on nitrogen at very low field is caused by the absence of paramagnetic effects in protonated species[3c] which accounts also for the higher shifts of γ and β hydrogens as compared with those of α protons. The methyl hydrogens of acetylpyridinium are slightly shifted to low field in SO₂ solution. The hydrogens of the pyridinium ring are differently affected by protonation and this depends on the position of the substituent in the ring.

In 4-acetyl- and 4-benzoylpyridine, protonation of the nitrogen deshields the 3 and 5 positions more than the 2 and 6 positions. In the 2 and 3 isomers the effect of protonation is complicated by a solvent effect. The comparative displacements observed are summarized in Tables I and II.

Protonation of 2-, 3-, and 4-acetyl- and -benzoylpyridinium was shown to occur in the strong acid system, FSO₃H–SbF₅–SO₂. The protons on nitrogen and on oxygen were observed at low field in the nmr spectra at −60°. The existence of stereoisomers was confirmed by the observation of two OH peaks for the diprotonated 3- and 4-substituted pyridines. These isomers are explained by the assumption that the proton on oxygen of an asymmetrically substituted ketone[6] is in two magnetically nonequivalent environments depending on its relationship to the substituents. An equilibrium of two isomers is shown in Figures 1–4. Further evidence of the presence of two isomers was found in the coupling of the proton on oxygen with the methyl hydrogens in the diprotonated 3-acetyl- and 4-acetylpyridines. The low-field peak of the =OH⁺ in these isomers is split into a quartet by the neighboring methyl which appears as a doublet. The coupling is of the allylic type with the *cis* coupling constant bigger than the *trans*. The upfield peak of the =OH⁺ in the diprotonated 3-acetyl- or 4-acetylpyridines is a singlet where no *trans* allylic coupling is observable.

The spectrum of protonated 2-acetyl- and 2-benzoylpyridinium ions does not show the presence of two stereoisomers. It seems likely that the influence of the

(1) Part XLV: C. A. Cupas, J. M. Bollinger, and G. A. Olah, *J. Am. Chem. Soc.*, in press.

(2) National Institutes of Health Postdoctoral Research Investigator, 1966–1967.

(3) (a) I. C. Smith and W. G. Schneider, *Can. J. Chem.*, **39**, 1158 (1961); (b) G. Kotowycz, T. Schaefer, and E. Bock, *ibid.*, **42**, 2541 (1964); (c) V. M. S. Gil and J. N. Murrell, *Trans. Faraday Soc.*, **60**, 248 (1964).

(4) V. J. Kowalewski and D. G. de Kowalewski, *J. Chem. Phys.*, **37**, 2608 (1960).

(5) V. J. Kowalewski and D. G. de Kowalewski, *ibid.*, **36**, 267 (1959).

(6) G. A. Olah, M. Calin, and D. H. O'Brien, *J. Am. Chem. Soc.*, **89**, 3586 (1967).

Table I. Nmr Chemical Shifts of 2-, 3-, and 4-Acetylpyridines, -pyridinium Ions, and Protonated -pyridinium Ions

	H_2	H_3	H_4	H_5	H_6	CH_3	$=OH^+$	NH^+
2-Acetylpyridine[a]		−8.0	−7.8	−7.5	−8.7	−2.7		
2-Acetylpyridinium ion[b]		−8.9	−8.7	−8.3	−9.2	−2.8		−14.5[h]
		$\Delta\delta_4 \equiv \Delta\delta_3 > \Delta\delta_5 > \Delta\delta_6$						
Protonated 2-acetyl-pyridinium ion[c]		−9.7	−9.7	−9.4	−9.7	−4.0	−17.4	−13.9[h]
		$\Delta\delta_5 > \Delta\delta_4 > \Delta\delta_3 > \Delta\delta_6$						
3-Acetylpyridine[a]	−9.2	...	−7.5	−8.2	−8.8	−2.7		
3-Acetylpyridinium ion[b]	−9.1	...	−8.2	−8.8	−9.0	−2.7		−14.8[h]
		$\Delta\delta_4 > \Delta\delta_5 > \Delta\delta_6 > \Delta\delta_2$						
Protonated 3-acetyl-pyridinium ion[c]	−10.0	...	−9.0	−9.7	−10.0	−4.0[d]	−16.0[e] −15.0	−13.2[h]
		$\Delta\delta_6 > \Delta\delta_5 \equiv \Delta\delta_2 > \Delta\delta_4$						
4-Acetylpyridine[a]	−8.5	−7.4	...	−7.4	−8.5	−2.4		
4-Acetylpyridinium ion[b]	−8.8	−8.4	...	−8.4	−8.8	−2.7		−14.8[h]
		$\Delta\delta_3 \equiv \Delta\delta_5 > \Delta\delta_2 \equiv \Delta\delta_6$						
Protonated 4-acetyl-pyridinium ion[c]	−9.6	−9.4	...	−9.4	−9.6	−4.0[f]	−16.5[g] −16.3	−13.3[h]
		$\Delta\delta_3 \equiv \Delta\delta_5 > \Delta\delta_2 \equiv \Delta\delta_6$						

[a] In $CDCl_3$ at room temperature. [b] In SO_2 at −60°. [c] In SO_2–SbF_5–FSO_3H at −60°. [d] Doublet, $J_{CH_3-OH} = 0.9$ Hz. [e] Quartet, $J_{OH-CH_3} = 0.9$ Hz. [f] Doublet, $J_{CH_3-OH} = 1.0$ Hz. [g] Quartet, $J_{OH-CH_3} = 1.0$ Hz. [h] Broad peak.

Table II. Nmr Chemical Shifts of 2-, 3-, and 4-Benzoylpyridines, -pyridinium Ions, and Protonated -pyridinium Ions

	H_2	H_3	H_4	H_5	H_6	Ph	$=OH^+$	NH^+
2-Benzoylpyridine[a]	...	−8.2	−8.0	−7.9	−8.6	−7.4		
2-Benzoylpyridinium ion[b]	...	−8.6	−8.2	−8.1	−8.9	−7.4		−14.7[d]
		$\Delta\delta_3 > \Delta\delta_6 > \Delta\delta_4 \equiv \Delta\delta_5$						
Protonated 2-benzoyl-pyridinium ion[c]	...	−9.5	−9.3	−9.2	−9.8	−8.7	−14.7	−13.5[d]
		$\Delta\delta_4 \equiv \Delta\delta_5 > \Delta\delta_3 \equiv \Delta\delta_6$						
3-Benzoylpyridine[a]	−9.0	...	−7.1	−8.1	−8.8	−7.6		
3-Benzoylpyridinium ion[b]	−8.9	...	−8.2	−8.8	−8.9	−7.6		−15.2[d]
		$\Delta\delta_4 > \Delta\delta_5 > \Delta\delta_6 > \Delta\delta_2$						
Protonated 3-benzoyl-pyridinium ion[c]	−9.6	...	−9.0	−9.6	−9.6	−8.6	−14.2 −13.9	−13.2[d]
		$\Delta\delta_4 \equiv \Delta\delta_5 > \Delta\delta_2 \equiv \Delta\delta_6$						
4-Benzoylpyridine[a]	−8.7	−7.7	...	−7.7	−8.7	−7.5		
4-Benzoylpyridinium ion[b]	−8.9	−8.2	...	−8.2	−8.9	−7.6		−15.1[d]
		$\Delta\delta_3 \equiv \Delta\delta_5 > \Delta\delta_2 \equiv \Delta\delta_6$						
Protonated 4-benzoyl-pyridinium ion[c]	−9.6	−8.9	...	−8.9	−9.6	−8.7	−14.5 −14.1	−13.4[d]
		$\Delta\delta_3 \equiv \Delta\delta_5 > \Delta\delta_2 \equiv \Delta\delta_6$						

[a] In $CDCl_3$ at room temperature. [b] In SO_2 at −60°. [c] In SO_2–SbF_5–FSO_3H at −60°. [d] Broad peak.
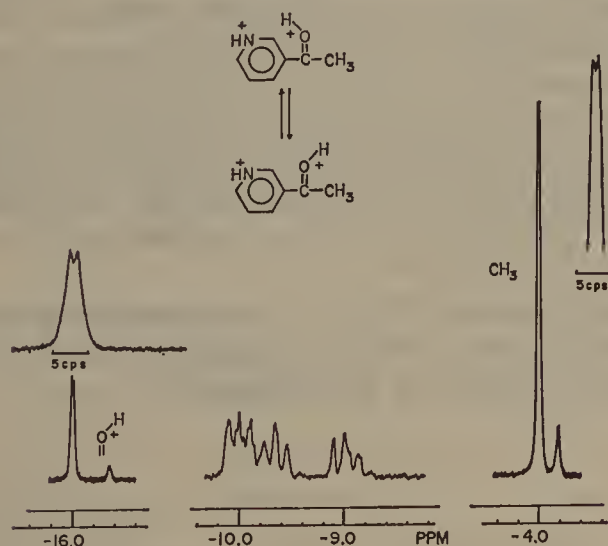
Figure 1.

Figure 2.

near positive charge on the nitrogen stabilizes the conformation shown in Figures 5 and 6. The proximity of the positive charge also highly deshields the proton on oxygen which appears at very low field, −17.4 ppm, for diprotonated 2-acetylpyridine. The positive charge in this case is necessarily located on the oxygen atom and not on the carbon atom of the carbonyl group. Diprotonated 2-benzoylpyridine shows the proton on oxygen at higher field. The smaller deshielding observed could be explained by the phenyl substituent effect in which a part of the positive charge is now strongly delocalized. The methyl shifts in the isomeric, diprotonated acetylpyridines are about equal, whereas the phenyl shifts in diprotonated 2-phenylpyridine are 0.3 and 0.2 ppm downfield from the 3- and 4-benzoyl isomers, respectively. The effect of the positive charge on oxygen on the chemical shifts of the pyridinium ring hydrogens is generally greater on the *para* than the *ortho* and *meta* positions relative to the substituent. The comparative displacements are summarized in Tables I and II.
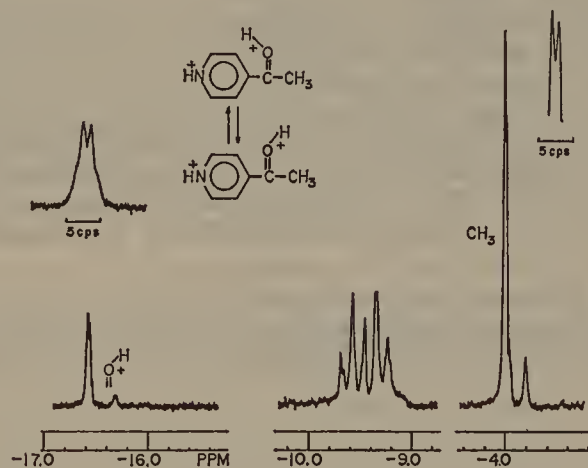
Diprotonation of the acetyl- and benzoylpyridines shifts the resonance position of the hydrogens on nitro-
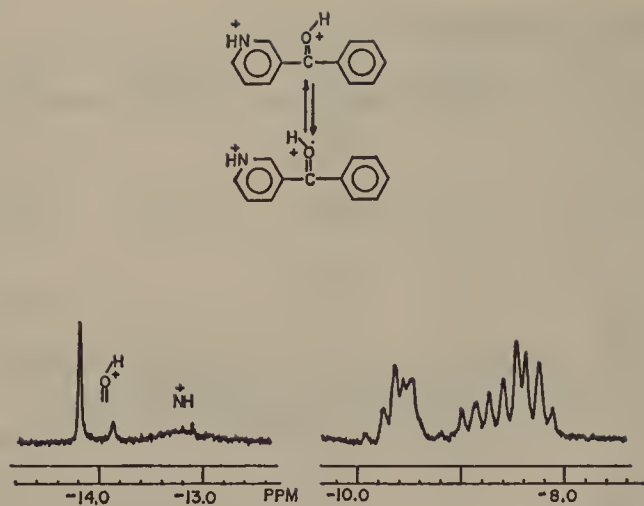
Figure 3.
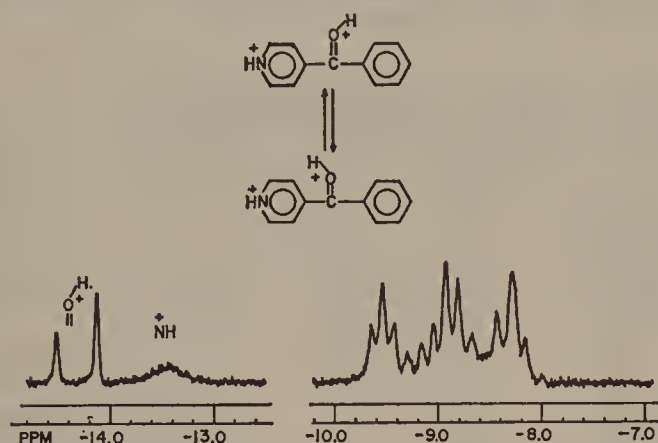
Figure 4.

Figure 5.

Figure 6.

gen upfield slightly compared with those of mono-protonated species in the same solvent at −60° (Tables I and II).

Experimental Section

Materials. The 2-, 3-, and 4-acetyl- and -benzoylpyridines were commercially available and were distilled or recrystallized before use. The acylpyridinium hydrochloride salts were prepared by bubbling a stream of dry hydrogen chloride through a chloroform solution of free base. The melting points of the salts recrystallized from chloroform agree with the literature values: I, 2-acetylpyridinium hydrochloride, 184–185°;[7] II, 3-acetylpyridinium hydrochloride, 178°;[8] III, 4-acetylpyridinium hydrochloride, 155°; IV, 2-benzoylpyridinium hydrochloride, 128°;[9] V, 3-benzoylpyri-

dinium hydrochloride, 161°;[9] and VI, 4-benzoylpyridinium hydrochloride, 197°.[9]
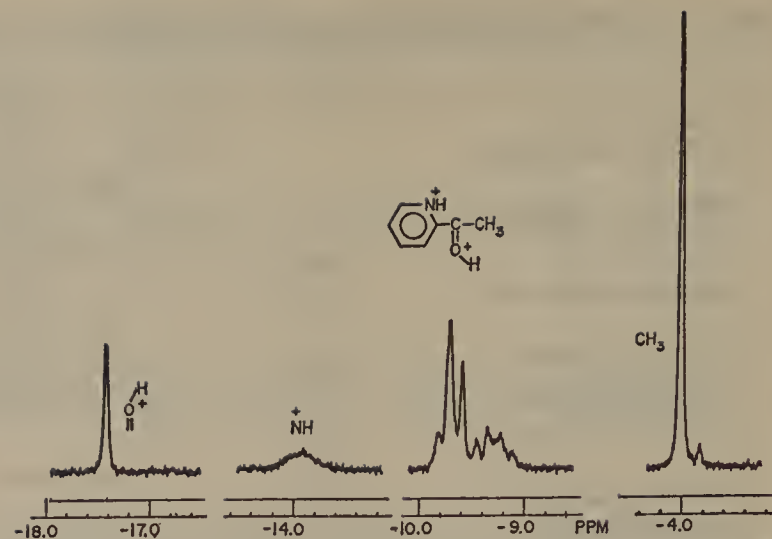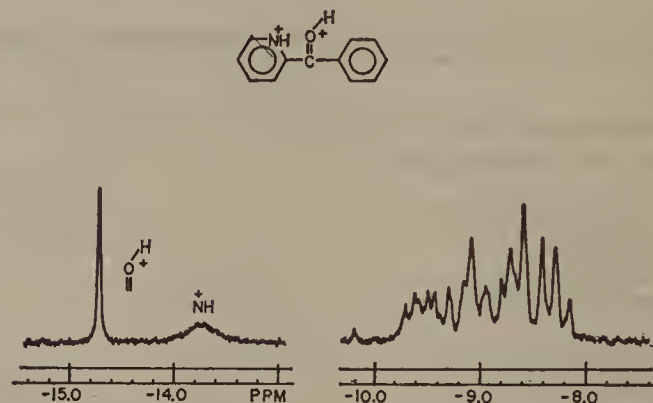
Nmr Spectra. A Varian Associates Model A-56-60 A spectrometer with a variable-temperature probe was used for all spectra. External TMS was used as reference (sealed capillary tube). The coupling constants are accurate to within 0.1 Hz.

Samples of protonated acetyl- and benzoylpyridinium were prepared by dissolving 0.2–0.3 g of the acylpyridinium hydrochloride in 1.5 ml of sulfur dioxide held at −76°. This solution was added dropwise to 1.5 ml of HSO_3F–SbF_5 (1:1 M solution) dissolved in 1 ml of cold sulfur dioxide. The excess of acid was always indicated in the spectra by the intense peak at −10.9 ppm. This peak and that of the H_3O^+ at about −10.5 ppm were deleted from the spectra (Figures 1–6) for simplicity.

(7) A. Ginner, *Ber.*, **34**, 4240 (1901).
(8) L. Musajo and M. Colonna, *Gazz. Chim. Ital.*, **62**, 894 (1932).
(9) K. E. Crook and S. M. McElvain, *J. Am. Chem. Soc.*, **52**, 4006 (1930).

Stable Carbonium Ions. XLVII.[1] Alkylcarbonium Ion Formation from Alkanes *via* Hydride (Alkide) Ion Abstraction in Fluorosulfonic Acid–Antimony Pentafluoride–Sulfuryl Chlorofluoride Solution[2]

George A. Olah and Joachim Lukas[3]

Contribution from the Department of Chemistry, Case Western Reserve University, Cleveland, Ohio 44106. Received April 21, 1967

Abstract: Alkylcarbonium ions are formed at temperatures between -125 and $+25°$ from alkanes *via* hydride (alkide) ion abstraction in fluorosulfonic acid–antimony pentafluoride solution (diluted at lower temperatures with sulfuryl chlorofluoride). All alkylcarbonium ions convert ultimately on heating through isomerization, fragmentation, and dimerization to the *t*-butyl cation which was found to be stable in the acid solution up to 150°.

Hydride ion abstraction is primarily known as transfer of a hydride ion between a hydrocarbon and a carbonium ion. This could occur intramolecularly in a rearrangement or intermolecularly as in the case of the formation of tropylium ion from triphenylcarbonium ion and tropylidene.[4] Isomerizations of saturated hydrocarbons catalyzed by Friedel–Crafts catalysts (HF–BF$_3$, HCl–AlCl$_3$) show evidence (evolution of H$_2$, rate dependence on H_0) of hydride ion abstraction as initiating steps.[5] Claims that Lewis acid halides themselves are capable of effecting hydride ion abstraction in the absence of proton sources were disproved by Nenitzescu.[6]

A more recent claim of the ability of antimony pentachloride to abstract hydride ion[7] may also find its explanation in traces of proton impurities in the reaction medium.[8]

We have previously reported the generation of stable alkylcarbonium ions from alkyl halides in SbF$_5$ and SbF$_5$–SO$_2$ solutions[9] and from alcohols in FSO$_3$H–SbF$_5$ solution.[10] We would like now to report our observations relating to the generation of alkylcarbonium ions from alkanes *via* hydride (alkide) ion abstraction with the extremely strong acid FSO$_3$H–SbF$_5$.

$$R_3CH \xrightarrow{\text{FSO}_3\text{H–SbF}_5} R_3C^+ \text{SbF}_5\text{FSO}_3^- + H_2$$

Results and Discussion

n-Butane and isobutane both form exclusively the *t*-butyl cation (I) (sharp singlet at -4.50 ppm[9]) when dissolved in FSO$_3$H–SbF$_5$ solution. The *t*-butyl cation is, in our experience, the most stable alkylcarbonium ion. When generated in FSO$_3$H–SbF$_5$ solution *via* hydride ion abstraction, the solution of I is unchanged even after having been heated to 150°. All other investigated alkylcarbonium ions were observed to convert to ion I at higher temperatures through various fragmentation (and isomerization) pathways.

$$(CH_3)_3CH \longrightarrow \underset{I}{(CH_3)_3C^+} \longleftarrow CH_3CH_2CH_2CH_3$$
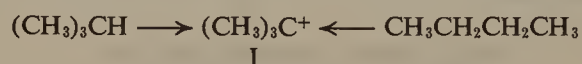
The increasing viscosity of the neat fluorosulfonic acid–antimony pentafluoride mixture puts a lower limit of 0–10° on the heterogeneous reaction. It therefore was necessary to use a solvent to dilute the solution and also to lower the freezing point. Sulfur dioxide was used extensively in stable carbonium ion chemistry previously as solvent, but had its disadvantages. The melting point is, in some cases, too high ($-75°$); the carbonium ions are considerably less stable in solutions diluted with SO$_2$ than in undiluted acid. In some cases carbonium ions react with SO$_2$ to give sulfinic acids. Sulfuryl chlorofluoride (SO$_2$ClF) was found to be a more suitable solvent. It dissolves hydrocarbons to a certain extent, and solutions of carbonium ions in FSO$_3$H–SbF$_5$ diluted with it are stable even at higher temperatures (-30 to $0°$). The solutions are colorless. However, compared to similar solutions in SO$_2$, the spectra of carbonium ions in SO$_2$ClF do not show the same degree of resolution. The melting point of SO$_2$ClF is $-125°$, 50° lower than that of SO$_2$. Carbonium ion chemical shifts show dependence on solvent and acidity of the system. In the case of trimethylcarbonium ion, its nmr singlet moves downfield with increasing acid concentration (-4.2 ppm in 1:1 SO$_2$ClF:FSO$_3$H–SbF$_5$ and -4.5 ppm in neat FSO$_3$H–SbF$_5$).

n-Pentane and isopentane are ionized in FSO$_3$H–SbF$_5$ to the *t*-amyl cation[9] II. At $-30°$ the pmr spectrum shows a methyl triplet at -4.42 ppm (with the large long-range coupling $^4J_{\text{H–H}} = 5.0$ Hz through the sp^2-hybridized carbonium ion carbon atom), methylene multiplet at -4.75 ppm, and the methyl triplet at -2.17 ppm ($^3J_{\text{H–H}} = 5.6$ Hz).

$$\underset{\underset{CH_3}{|}}{CH_3CHCH_2CH_3} \longrightarrow \underset{\underset{CH_3}{|}}{CH_3\overset{+}{C}CH_2CH_3} \longleftarrow CH_3CH_2CH_2CH_2CH_3$$
$$\text{II}$$

(1) Part XLVI: G. A. Olah and M. Calin, *J. Am. Chem. Soc.*, **89**, 4736 (1967).

(2) For a preliminary communication see G. A. Olah and J. Lukas, *ibid.*, **89**, 2227 (1967).

(3) National Institutes of Health Postdoctoral Research Investigator, 1965–1967.

(4) For a comprehensive review on intermolecular hydride abstraction, see (a) N. C. Deno, J. Peterson, and George S. Saines, *Chem. Rev.*, **60**, 7 (1960); (b) C. D. Nenitzescu in "Carbonium Ions," G. A. Olah and P. von R. Schleyer, Ed., Interscience Publishers, Inc., New York, N. Y., 1967.

(5) "Friedel–Crafts and Related Reactions," Vol. I, G. A. Olah, Ed., Interscience Publishers Inc., New York, N. Y., 1963, p 86.

(6) C. D. Nenitzescu and J. P. Cantuniari, *Ber.*, **66**, 1097 (1933).

(7) J. Holms and R. Pettit, *J. Org. Chem.*, **28**, 1695 (1963).

(8) Observations of Dr. Paul Kreienbühl in our laboratories.

(9) G. A. Olah, E. B. Baker, J. C. Evans, W. S. Tolgyesi, J. S. McIntyre, and I. J. Bastian, *J. Am. Chem. Soc.*, **86**, 1360 (1964); G. A. Olah, M. B. Comisarow, C. A. Cupas, and C. U. Pittman, Jr., *ibid.*, **87**, 2997 (1965).

(10) G. A. Olah, M. B. Comisarow, C. A. Cupas, and C. U. Pittman, Jr., *ibid.*, **87**, 2997 (1965).
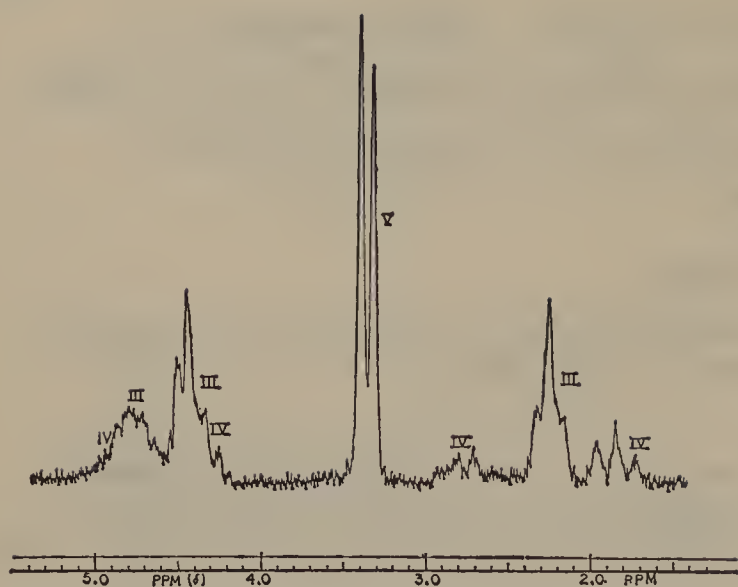
Figure 1. Mixture of *t*-hexyl cations: methyldiethylcarbonium ion (III), dimethyl-*n*-propylcarbonium ion (IV), and dimethylisopropylcarbonium ion (V).

With increasing temperature the methyl peaks start to coalesce until they collapse at 90° to give a single broad peak at −3.60 ppm. The methylene peak is unchanged. The observed temperature dependence of the spectrum of II indicates equilibration at elevated temperatures.

$$CH_3\overset{+}{C}CH_2CH_3 \rightleftharpoons CH_3CH_2\overset{+}{C}CH_3$$
$$||$$
$$CH_3 CH_3$$
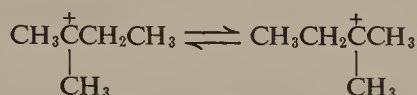
To explain equilibration, an equilibrium between the *t*-amyl cation (dimethylethylcarbonium ion) (IIa) and the secondary methylisopropylcarbonium ion (IIIa) must exist through a 1,2-hydride shift. The latter (IIIa) can react by reversing the hyride shift (IIIa → IIa) or by undergoing a methyl shift to give the equilibrating methylisopropylcarbonium ion (IIIa ⇆ IIIb). A 1,2-hydride shift of IIIb gives a *t*-amyl cation in which scrambling of the methyl groups has occured.
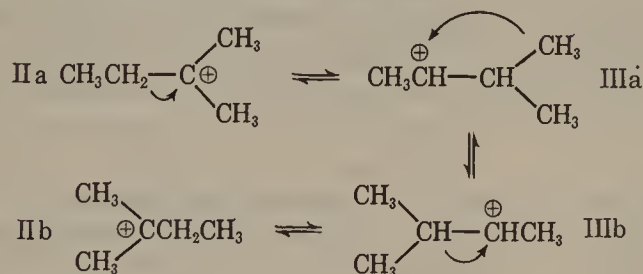
The temperature of collapse of the two methyl peaks is −10° in SO₂[9] or SO₂ClF solution, thus 100° lower than in undiluted acid (+90°). Obviously ion pairing is more intimate in the latter case, thus obstructing methyl and hydride shifts.

At 150° the rate of decomposition of II to I is still slow. These observations seem to indicate remarkable stabilization of alkylcarbonium ions in the highly acidic solvent, involving in all probability solvation of tight ion pairs.

The ionization pattern of neopentane differs sharply with temperature. At −20° in FSO₃H–SbF₅–SO₂ClF, it slowly loses a primary hydrogen. The incipient primary carbonium ion rearranges immediately to the *t*-amyl cation (II). At +25° however, without solvent, the *t*-butyl ion (I) is formed exclusively while methane is liberated (as proved by mass spectroscopic analysis).
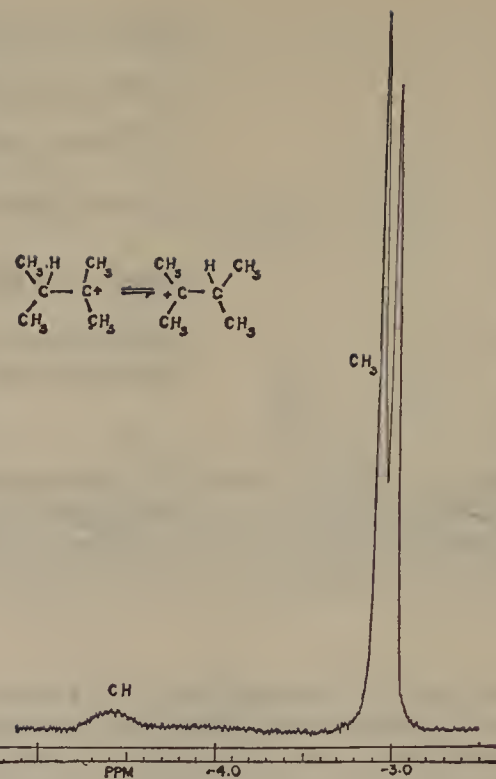
Figure 2. Dimethylisopropylcarbonium ion (V).

Thus at higher temperatures abstraction of methide ion giving the *t*-butyl cation is favored over hydride ion abstraction. That ion I was not formed *via* ion II is seen from the fact that II is stable up to 150°.
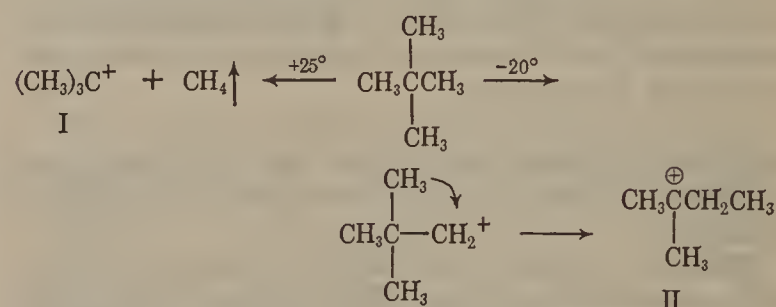
n-Hexane, 2-methylpentane, 3-methylpentane, 2,2-dimethylbutane, and 2,3-dimethylbutane all show in FSO₃H–SbF₅ solution at room temperature a spectrum (Figure 1) consisting of all three isomeric tertiary hexyl cations: the methyldiethylcarbonium ion (III), the dimethyl-*n*-propylcarbonium ion (IV), and the dimethylisopropylcarbonium ion (V) (see Scheme I). On heating, ions III and IV are increasingly converted into ion V, which seems to be the most stable hexyl cation. The *t*-hexyl cations convert to the *t*-butyl cation (I) above 80°.

The ionization of the isomeric hexanes in FSO₃H–SbF₅–SO₂ClF solution below −60° gives the unrearranged *t*-hexyl cations.
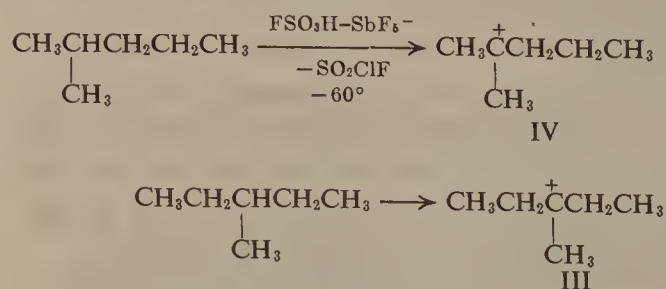
The dimethylisopropylcarbonium ion (V) is particularly interesting (Figure 2). It is an example of an acyclic equilibrating carbonium ion.[11]

(11) P. von R. Schleyer, W. Watts, R. C. Fort, M. Comisarow, and G. A. Olah, *J. Am. Chem. Soc.*, 86, 5679 (1964).

Scheme I

$$CH_3CH_2CH-CH_2CH_3 \quad CH_3CH-CHCH_3 \quad CH_3CH_2CCH_3$$

(Scheme I structures)

III

V

IV

$$CH_3CH-CHCH_3 \rightarrow CH_3CH-\overset{+}{C}CH_3 \rightleftarrows CH_3\overset{+}{C}-CHCH_3$$
$$\qquad\qquad V$$
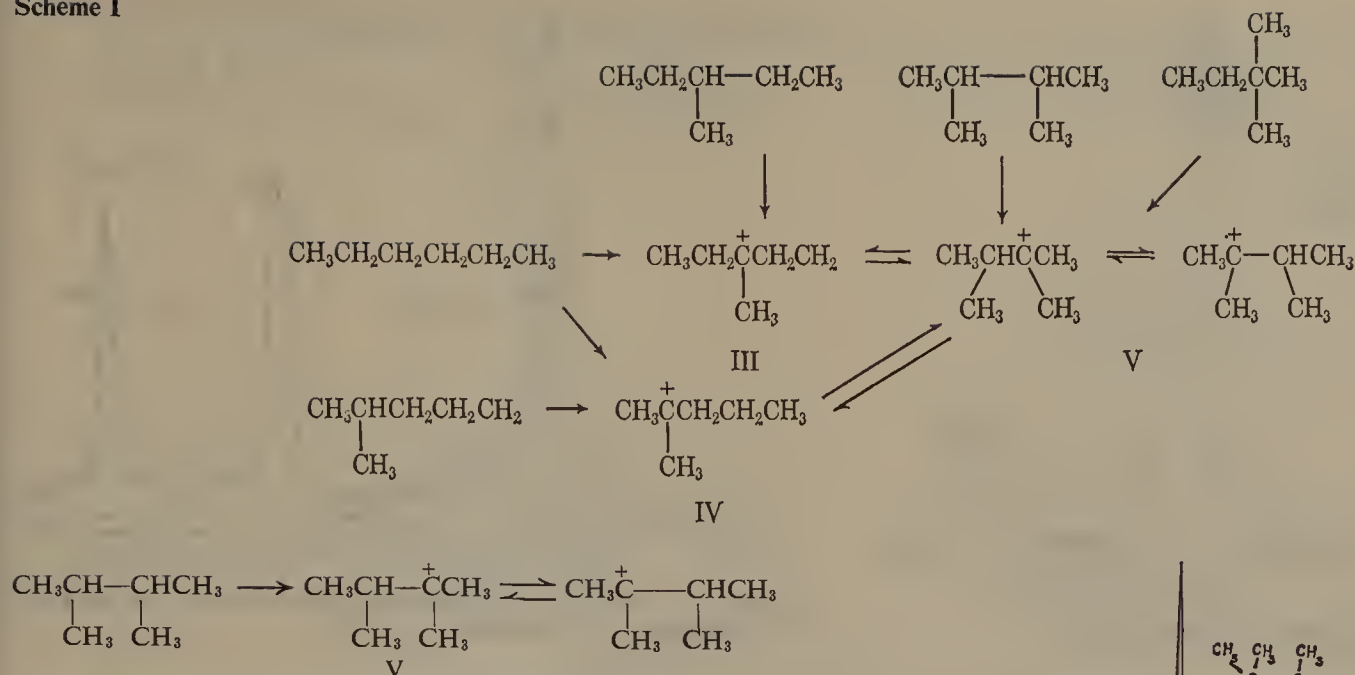
The four methyl groups are equivalent, found as a doublet at -3.32 ppm ($J_{H-H} = 4.2$ Hz). They must therefore be coupled equally to one proton. Whether the ion is equilibrating rapidly or is a static "nonclassical ion" can be determined by interpreting the observed
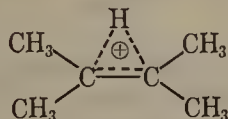
deshielding of the methyl protons and that of the methine proton in the nmr spectrum. The methine proton is at -4.40 ppm, and it could be shown to be coupled to the doublet of the methyl group by spin–spin decoupling. On comparison with static carbonium ions this chemical shift is as would be expected for a tertiary hydrogen on a carbon atom α to the positive center. A nonclassical structure, in which the hydrogen should be carrying part of the positive charge or in which it would be partially bonded to a positively charged carbon atom, is therefore unlikely.[12]

Ionization of isomeric heptanes in $FSO_3H-SbF_5-SO_2ClF$ resulted in the observation of three tertiary heptyl cations. 2,2,3-Trimethylbutane in $FSO_3H-SbF_5-SO_2ClF$ at $-60°$ gives the dimethyl-t-butylcarbonium ion (VI) which shows a single sharp nmr singlet (-2.86 ppm). A fast 1,2-methyl shift must equilibrate all five methyl groups (Figure 3).

$$CH_3CH-\overset{CH_3}{\underset{CH_3}{C}}CH_3 \rightarrow CH_3\overset{+}{C}-\overset{CH_3}{\underset{CH_3}{C}}CH_3 \rightleftarrows CH_3\overset{CH_3}{C}-\overset{+}{C}CH_3$$
$$\qquad\qquad\qquad VI$$
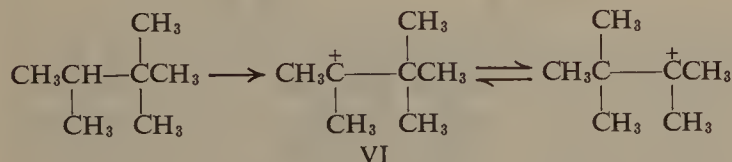
The fact that there is only one singlet and the chemical shift is similar to that of the dimethylisopropylcarbonium ion excludes a static nonclassical ion such as
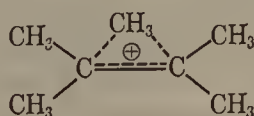
This conclusion is further enhanced by the comparison of the deshielding of the methyl groups compared

(12) The α-hydrogen in the isopropyl ion appears at -13.5 ppm; see ref 9.
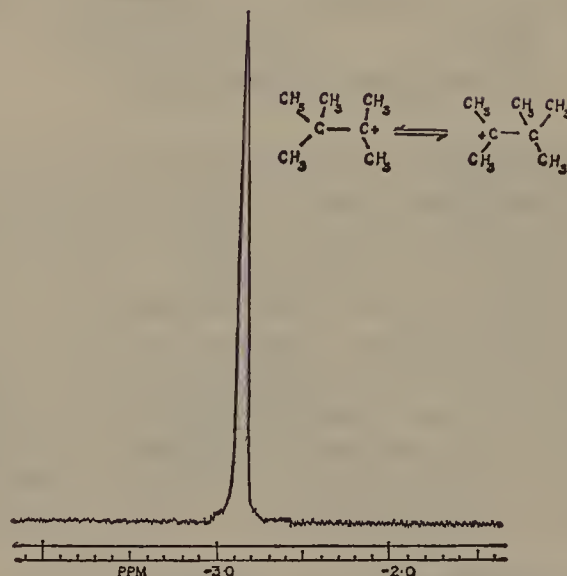
Figure 3. Dimethyl-t-butylcarbonium ion (VI).

with recently observed bridged tetramethylethylene halonium ions.[13] The deshielding of the methyl protons of ion VI compared with the methyl protons in 2,2,3,3-tetramethylbutane is 2.00 ppm. This deshielding is much larger than observed in bridged tetramethylethylene halonium ions (0.95–0.75 ppm).

$$X = I, Br, Cl$$
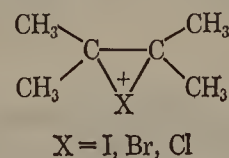
If ion VI would be the bridged nonclassical ion (a protonated tetramethylcyclopropane) the four methyl groups would be expected at much higher field partly because of charge delocalization on the cyclopropane ring, partly because of the expected anisotropy effect.

It is interesting to note that the rate of the 1,2-methyl shift even at $-180°$ is still extremely fast and no change in the single line spectrum is observed.[14] This would mean, in comparison with our previous observation of fast shifts in the norbornyl ion,[15] a rate probably exceeding 5×10^3 sec^{-1} and a barrier of less than 2–3 kcal/mole.[16]

(13) G. A. Olah and J. M. Bollinger, *J. Am. Chem. Soc.*, **89**, 4744 (1967).
(14) Observation of Dr. E. Namanworth.
(15) M. Saunders, P. von R. Schleyer, and G. A. Olah, *J. Am. Chem. Soc.*, **86**, 5680 (1964).
(16) In cooperation with Professor E. Namanworth and Professor M. Saunders, an effort is being made to measure the rate of methyl shift by spin–echo techniques.
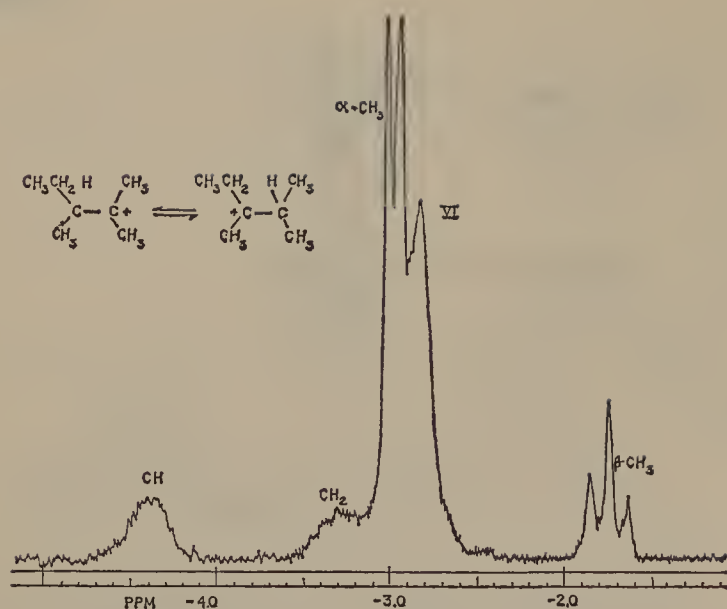
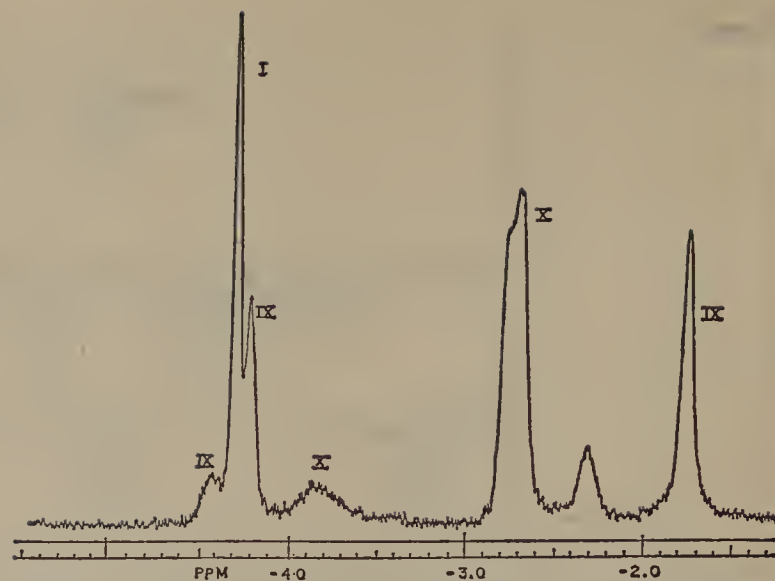Figure 4. Dimethylisobutylcarbonium ion (VII).

Figure 5. Mixture of dimethylneopentylcarbonium ion (IX) and dimethyl-*sec*-pentylcarbonium ion (X).

In FSO₃H–SbF₅–SO₂ClF, 2,4-dimethylpentane gives a spectrum which is dominated by a doublet (−2.96 ppm). In addition there is a triplet (−1.75 ppm) and two multiplets (−4.35 ppm and −3.30 ppm). Spin–spin decoupling shows that the multiplet at −4.35 ppm and the doublet at −2.96 ppm are coupled as is the multiplet at −3.30 ppm and the triplet at −1.75 ppm. These data indicate rapid 1,2-hydride and methyl shifts to give the equilibrating dimethylisobutyl cation (VII) (Figure 4). The spectrum also shows an absorption peak at −2.86 ppm indicating some isomerization to ion
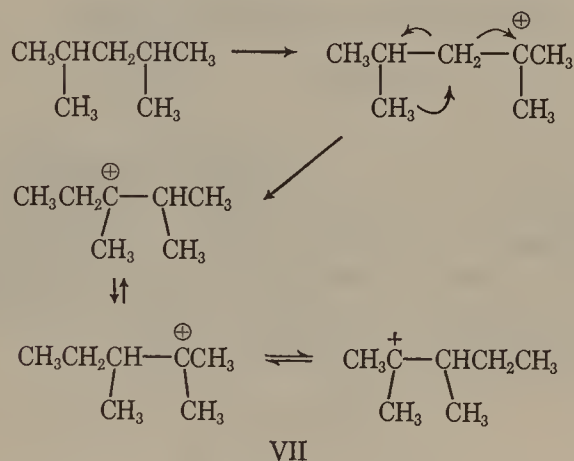
VI. In ion VII the methylene group (multiplet at −3.30 ppm) is coupled to the β-methyl group (triplet at −1.75 ppm). The equilibrating hydrogen (multiplet at −4.35 ppm) is coupled to the three α-methyl groups (doublet at −2.96 ppm) and to the methylene group (multiplet at −3.30 ppm).

3-Ethylpentane at −60° is ionized to the expected triethylcarbonium ion (VIII). The nmr spectrum shows
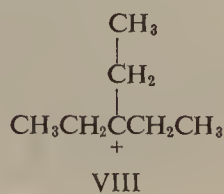
two broadened peaks in the ratio 2:3. Fine structure could not be observed.

Isomeric octanes ionize to stable octyl cations without fragmentation only below −80°. At higher temperature, fragmentations eventually leading to the *t*-butyl cation take place.

In 2,2,3,3-tetramethylbutane, cleavage occurs at temperatures above −40°.
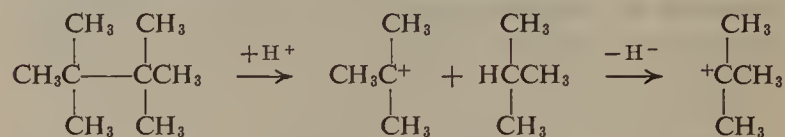
Isooctane (2,2,4-trimethylpentane) ionizes at −100° to give a spectrum with peaks at −4.32 (a), −4.13 (b), and −1.51 (c) ppm. A static, nonequilibrating isooctyl cation (IX) is consistent with this spectrum.
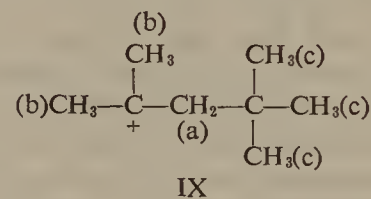
2,3,4-Trimethylpentane, at −100°, in FSO₃H–SbF₅–SO₂ClF solution, shows a dominating broad peak at −2.60 ppm. An equilibrating ion X involving successive 1,2-hydrogen shifts can explain this spectrum. All methyl groups give rise to the peak at −2.60 ppm and the two tertiary hydrogen atoms to that at −3.72 ppm.
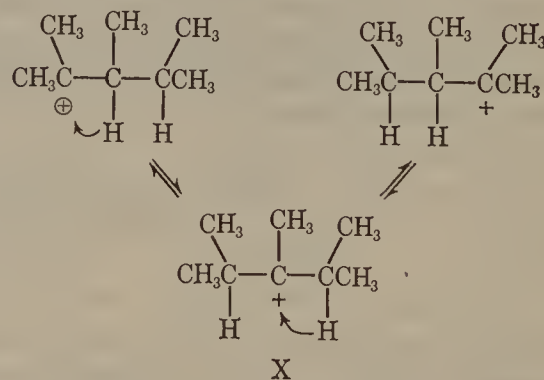
Even at −100°, the spectral pattern of ion IX starts to appear in the spectrum of ion X and *vice versa*. Also the singlet for ion I (trimethylcarbonium ion) is present (Figure 5). At −90° X and IX rearrange to one another to give a mixture of varying composition. However, ion X seems to be somewhat more stable. Above −80° the mixture cleaves to give ion I exclusively. The nmr data of all observed alkylcarbonium ions are summarized in Table I.

Table I. Nmr Shifts and Coupling Constants of Alkylcarbonium Ions

Carbonium ion	Structure	δ, ppm in SO$_2$ClF (J_{HH}, Hz)	Temp, °C	Rearr or cleaves to
Trimethyl (I)	CH$_3$ \ $\overset{+}{C}$ / CH$_3$ | CH$_3$	4.20^a	+150	
Dimethylethyl (II)	CH$_3$CH$_2$$\overset{+}{C}$ (a) (b) \ CH$_3$ (c) | CH$_3$	a 1.94 (tr, 5.2) b 4.42 (m, 5.2), 4.42 (m, 5.2) c 4.02 (tr, 4.7), 3.60 (m)	−30 +150	I (~1 hr half-life)
Methyldiethyl (III)	(a) CH$_3$ | CH$_3$CH$_2$$\overset{+}{C}CH_2CH_3$ (b) (c)	a 4.16 (tr, 4.8) b 4.44 (q, 6.0) c 1.87 (tr, 6.0)	−20 +80	IV and V I
Dimethylpropyl (IV)	CH$_3$$\overset{+}{C}CH_2CH_2CH_3$ (b) (c) (d) | CH$_3$ (a)	a 4.05 (tr, 4.8) b 4.40 (q, 6.0) c 2.58 (m) d 1.43 (tr, 7.0)	−20 +80	III and V I
Dimethylisopropyl (V)	CH$_3$ \ (b) CH$_3$ $\overset{+}{C}$CH $\rightleftharpoons$ CHC / \ CH$_3$ CH$_3$ CH$_3$ CH$_3$ CH$_3$ CH$_3$	a 3.04 (d, 4.2) b 4.55 (m)	−20 +80	III and IV I
Dimethyl-t-butyl (VI)	CH$_3$ CH$_3$ CH$_3$ CH$_3$ $^+$CCCH$_3$ $\rightleftharpoons$ CH$_3$C$\overset{+}{C}$ / | | CH$_3$ CH$_3$ CH$_3$ CH$_3$	2.86 (s)	−10	I
Dimethylisobutyl (VII)	(a) CH$_3$ CH$_3$ CH$_3$ CH$_3$ CCH(b) $\rightleftharpoons$ CHC$^+$ / \ / \ CH$_3$ CH$_2$CH$_3$ CH$_3$ CH$_2$CH$_3$ (c) (d)	a 2.96 (d, 4.1) b 4.35 (m) c 3.30 (m) d 1.75 (tr, 6.5)	−70	VI, always present
Triethyl (VIII)	CH$_3$ | CH$_2$ | CH$_3$CH$_2$$\overset{+}{C}CH_2CH_3$	a 1.88 (m) b 4.42 (m)	−70	VI
Dimethylneopentyl (IX)	(a) (c) CH$_3$ CH$_3$ (b) | CH$_3$$\overset{+}{C}$—CH$_2$—CCH$_3$ | CH$_2$	a 4.13 (br) b 4.32 (m) c 1.51 (s)	−100 −75	Rearr to X Cleaves to I
Methyldiisopropyl (X)	CH$_3$ CH$_3$ CH$_3$ CH$_3$ CH$_3$ CH$_3$ CH$_3$C——C——CCH$_3$ $\rightleftharpoons$ CH$_3$C——C——CCH$_3$ | | + (b) + | | H H H H (a)	a 3.85 (m) b 2.64 (d)	−100 75	Rearr to IX Cleaves to I

^{a} Abbreviations used are: s, singlet; d, doublet; tr, triplet; qu, quartet; q, quintuplet; m, multiplet; br, broad. All measured from external TMS capillary.

All the observed alkylcarbonium ions are tertiary. Abstraction of a secondary or primary hydrogen atom results in immediate rearrangement *via* 1,2-hydrogen or -methyl shifts or cleavage to give tertiary carbonium ions even at −100°. No evidence was found for reversible 1,3-hydride or -methyl shifts. Ease of ionization increases in the order: primary < secondary < tertiary hydrogen atoms. The secondary and tertiary systems undergo ionization at as low a temperature as −100°. Primary hydrogen atoms generally could not be ionized below −50°.

Methane does not ionize under the reaction conditions. It reacts only at +140° with FSO$_3$H–SbF$_5$ to give, as yet, unidentified products. *Ethane* gives a mixture of 90% I and 10% V through some dimerization and trimerization pathways.

Propane does not give the isopropyl cation in FSO$_3$H–SbF$_5$ solution, but gives immediately a mixture of the t-butyl ion (I) and the hexyl cations III, IV, and V. At temperatures where ionization takes place, fragmentation and isomerization are very fast.

At room temperature alkanes with seven or more carbon atoms are converted in the heterogeneous reaction with neat FSO$_3$H–SbF$_5$ to the t-butyl cation (I). At lower temperatures, however, their ions are more stable. Investigated examples are: *n*-heptane, 2,2,3-trimethylbutane, 3-ethylpentane, 2,4-dimethylpentane, 2-methylhexane, 2,3,4-trimethylpentane, 2,2,4-trimethylpentane, *n*-nonane, *n*-undecane, *n*-dodecane, and hexadecane. Even paraffin wax and polyethylene gave ion I. Obviously complex isomerization and fragmentation processes in the strong acid solution

lead ultimately to the very stable *t*-butyl cation (I). The tendency to cleave increases with the length and branching of alkanes. Butanes form the *t*-butyl cation (I) which is stable to 150° (boiling point of FSO₃H–SbF₅). Pentanes give the *t*-amyl cation IV which cleaves slowly to ion I at 150°, the hexyl cations cleave at +80°, the heptyl cations at −10°, and the octyl cations even at −80°.

In compounds with only primary hydrogen atoms (neopentane and 2,2,3,3-tetramethylbutane) a carbon–carbon bond is broken rather than a carbon–hydrogen bond. In ethane the fragmentation product would be CH_3^+, obviously less stable than $CH_3CH_2^+$, therefore a hydride ion is abstracted. The unstable ethyl cation then undergoes polymerization and cleavage. The difference with temperature in the fragmentation pattern of neopentane is striking. At low temperatures in a slow process, a primary hydrogen atom is abstracted. Above 0° a methide ion is abstracted (from a tertiary position) much faster than hydride ion (from a primary position).

The fate of the abstracted hydride ion is not yet fully determined in the reactions. In all probability it partly forms molecular hydrogen by adding to proton, part of which is observed escaping from the reaction mixture. The bulk of the nascent hydrogen, however, seems to reduce fluorosulfonic or fluoroantimonysulfonic acid.

Probably the most surprising observation of our work is that salts of the alkyl cations I, II, and V can be ob-tained and crystallized from SO_2 or SO_2ClF solutions at low temperature (−60 to −100°). They are stable at least to room temperature. Redissolved in SO_2 or SO_2ClF they give the unchanged nmr spectra of the ions. Attempts are in progress (with Professor M. Sundaralingam) for the X-ray crystallographic investigation of these alkylcarbonium salts.

Experimental Section

All nmr spectra were obtained on a Varian Associates Model A-56-60A nmr spectrometer. Spin–spin decoupling experiments were done on a Varian Associates Model HA-60 IL nmr spectrometer. External capillary TMS was used as reference.

Generation of Alkylcarbonium Ions in Neat FSO₃H–SbF₅ or HF–SbF₃. In a typical experiment, the alkane and a tenfold (weight) excess of acid (1:1 FSO₃H–SbF₅ or HF–SbF₅) were vigorously stirred at room temperature until they formed a homogeneous colorless mixture. The reaction is carried out with exclusion of moisture and is generally completed in 10–30 min. When using gaseous alkanes they are bubbled through the acid mixture in a slow stream.

Generation of Alkylcarbonium Ions in FSO₃H–SbF₅–SO₂ClF. To a 1:1 mixture of SO₂ClF with FSO₃H–SbF₅ or HF–SbF₅, the alkane is added. On mixing, it will generally ionize at temperatures above −120°. Nonionized material will be supernatant. If the acid concentration is decreased, nonionized alkane will be present in solution together with the carbonium ion.

Stable Carbonium Ions. XLVIII.[1a] Halonium Ion Formation *via* Neighboring Halogen Participation. Tetramethylethylene Halonium Ions

George A. Olah and J. Martin Bollinger[1b]

Contribution from the Department of Chemistry, Case Western Reserve University, Cleveland, Ohio 44106. Received April 21, 1967

Abstract: Bridged halonium ions were observed to arise on ionization of 2,3-dihalo-2,3-dimethylbutanes in antimony pentafluoride–sulfur dioxide solution at −60°, when the participating halogen atom is chlorine, bromine, or iodine. 2,3-Difluoro-2,3-dimethylbutane, on the other hand, gave α-fluoroisopropyldimethylcarbonium ion in which the fluorine atom is rapidly exchanging intramolecularly between the two equivalent sites. 2-Halo-3-acetoxy-2,3-dimethylbutanes and 2-halo-3-methoxy-2,3-dimethylbutanes also ionize in antimony pentafluoride–sulfur dioxide solution to similar ions. Bridged acetoxonium ion formation but not bridged methyloxonium ion formation is accompanying these ionizations.

Bromonium ion (I) formation in certain electrophilic additions of bromine to olefins is the generally accepted explanation for the complete stereospecificity observed.[2,3] This concept has been criticized be-cause it assumes that molecular rotation in a carbonium ion is much more rapid than attack by an external nucleophile, an assumption that was questioned.[4] Moreover, it has been suggested that rapidly equilibrating ions such as IIa and b could also lead to stereospecificity.[5] Similarly, from results of rate measurements and stereochemistry, bromine has been suggested as a good neighboring group, participating through the

(1) (a) Part XLVI: G. A. Olah and M. Calin, *J. Am. Chem. Soc.*, **89**, 4736 (1967). (b) National Science Foundation Postdoctoral Research Investigator, 1966–1967.

(2) We do not intend this brief introduction to be a comprehensive review of the literature on the mechanism of halogenation or neighboring halogen; for a more complete review on the latter, see B. Capone, *Quart. Rev.* (London), **18**, 45 (1964).
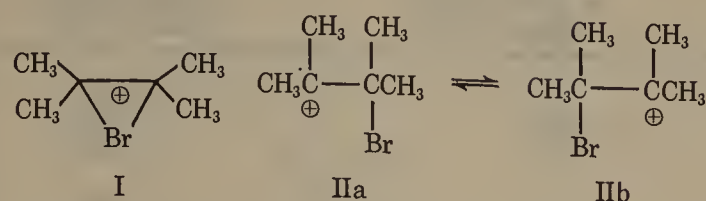
(3) Credit for this proposition is generally given to I. Roberts and G. E. Kimball, *J. Am. Chem. Soc.*, **59**, 947 (1937).

(4) B. M. Benjamin, H. J. Schaeffer, and C. J. Collins, *ibid.*, **79**, 6160 (1957).

(5) S. Winstein and B. K. Morse, *ibid.*, **74**, 1133 (1952).

same type of bridged bromium ions as suggested for bromination of olefins.[6]

I   IIa   IIb

Iodonium ions have been similarly suggested for iodination reactions,[7] and in reactions involving neighboring iodine.[8] The kinetic and stereochemical arguments are strong for a bridged intermediate.

It has been suggested that polar chlorination proceeds through a bridged chloronium ion,[9] although evidence has been presented that classical chlorocarbonium ions are also involved.[10] There seems to be no evidence that chlorine can give appreciable anchimeric assistance.[11]

Work on fluorination of olefins has led to the suggestion of classical fluorocarbonium ion intermediates.[12] A recent publication has also reported a 1,4-fluorine migration where a cyclic fluoronium ion has been proposed as either an intermediate or a transition state.[13] Generally, however, there is little indication of bridged fluoronium ion formation.

We wish now to report our results on the direct observation of tetramethylethylenehalonium ions in antimony pentafluoride–sulfur dioxide solution. We believe our results give the first direct experimental observation of halonium ions in solution.

Results and Discussion

Recently we succeeded in showing that β-anisylethyl, β-mesitylethyl, and β-(pentamethylphenyl)ethyl chloride ionize in antimony pentafluoride–sulfur dioxide solution at low temperature (−60°) via strong aryl participation to form the bridged arylonium (substituted phenonium) ions.
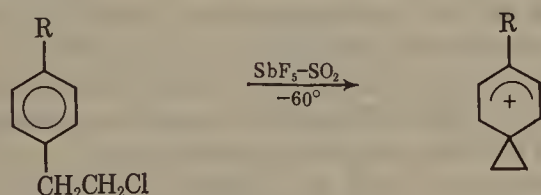
These arylonium ions were the first direct observation of bridged ions formed via π-neighboring group participation.

We now extend our investigations to bridged ions formed via n-neighboring group participation. When 2,3-dihalo-2,3-dimethylbutanes are ionized in antimony pentafluoride–sulfur dioxide solution at −60°, stable solutions of tetramethylethylenehalonium ions are obtained with chlorine, bromine, and iodine acting as donor-participating atoms. Fluorine in our experi-

(6) S. Winstein and H. J. Lucas, *J. Am. Chem. Soc.*, **61**, 1576, 2845 (1939).
(7) K. R. Wood, P. W. Kent, and D. Fisher, *J. Chem. Soc.*, 910 (1966); see also A. Hassner and C. Heathcock, *J. Org. Chem.*, **30**, 1748 (1965).
(8) S. Winstein, E. Grunwald, and L. L. Ingraham, *J. Am. Chem. Soc.*, **70**, 821 (1948).
(9) P. Ballinger and P. B. D. de la Mare, *J. Chem. Soc.*, 1481 (1957).
(10) P. B. D. de la Mare and A. Salama, *ibid.*, 3337 (1956).
(11) S. Winstein, *et al.*, *J. Am. Chem. Soc.*, **73**, 5458 (1951), and earlier papers; H. C. Brown, *Chem. Eng. News*, **45**, 87 (Feb 13, 1967).
(12) R. F. Merritt, *J. Am. Chem. Soc.*, **89**, 609 (1967).
(13) P. E. Peterson and R. J. Bopp, *ibid.*, **89**, 1283 (1967).

ments showed no similar ability and only rapidly equilibrating, open-chain classical fluorinated ions are obtained even at −90°.
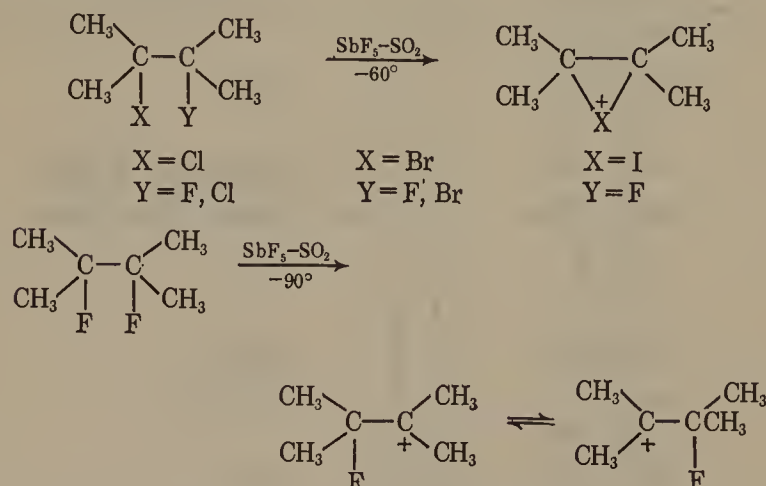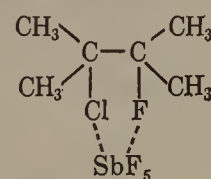

Table I summarizes pmr spectral data for the ions observed in antimony pentafluoride–sulfur dioxide solution. The covalent precursors and the products of methanolysis were observed in carbon tetrachloride solution.

The ionic nature of the halonium ions observed in the strong acid system is substantiated on the following basis: (1) downfield shifts of methyl groups of 0.8–1.8 ppm (donor–acceptor complexes would not be expected to be as strongly deshielded),[14] (2) disappearance of fluorine–proton coupling, (3) appearance of protonated methanol or acetic acid when the halonium ions are prepared by protonation of the appropriate methoxyl or acetyl derivatives (see subsequent discussion), and (4) solvolysis of the solutions which gives high yields of the expected quenched products.

Data of Table I apparently indicate that deshielding increases in going from chloronium to iodonium ion. This is the reverse of the expected trend based on the electronegativity of the halogen atoms. One would anticipate that iodine would better be able to bear positive charge and would, in the absence of other effects, be the least deshielded ion.[15] The comparison of the observed methyl deshielding effects, however, can be very misleading if one does not consider the effect of halogen atom on the methyl protons. That a large effect is operative is evident from the chemical shifts of the covalent starting halides. The effect is probably due to steric deshielding caused by the crowding introduced by the larger halogen atoms.[16] In Table II, therefore, we have presented differences in chemical shifts between the observed ions and covalent starting materials. In this comparison we have attempted to eliminate steric deshielding by comparing the ion with a suitable halogenated precursor. From

(14) Starting from unsymmetrical precursors rules out such a species as

(15) The methyl resonances of ethyl halides show the same trend, i.e., increased deshielding from F to I: H. Spiesecke and W. G. Schneider, *J. Chem. Phys.*, **35**, 722 (1961).
(16) T. Schaefer, W. F. Reynolds, and T. Yonemoto, *Can. J. Chem.*, **41**, 2969 (1963).

Table I. Pmr Resonance Data of Tetramethylethylene Halonium Ions and Their Dihalide Precursors and Methanolysis Products

| Compound	Starting material in CCl₄, intern. TMS	Ion in SbF₅–SO₂ at −60°, extern. TMS in DCCl₃	MeOH-quenched product in CCl₄, intern. TMS
H₃C CH₃ CH₃C—CCH₃ Cl Cl	−1.77(s)	−2.72(s)	−1.28(s) −1.52(s) −3.20(s)
H₃C CH₃ CH₃C—CCH₃ Cl F	−1.54(d) $J = 21$ Hz −1.57(d) $J = 1.1$ Hz	−2.72(s)	−1.28(s) −1.52(s) −3.20(s)
H₃C Cl CH₃C—CCH₃ H₃C Cl	−1.21(s) −2.12(s)	−2.72(s)	−1.28(s) −1.52(s) −3.20(s)
H₃C CH₃ CH₃C—CCH₃ Br Br	−2.00(s)	−2.86(s)	−1.35(s) −1.80(s) −3.24(s)
H₃C CH₃ CH₃C—CCH₃ Br F	−1.52(d) $J = 21$ Hz −1.78(d) $J = 1.0$ Hz	−2.86(s)	−1.35(s) −1.80(s) −3.24(s)
H₃C CH₃ CH₃C—CCH₃ I F	−1.54(d) $J = 21$ Hz −2.00(s)	−3.05(s)	−1.37(s) −1.87(s) −3.26(s)
H₃C CH₃ CH₃C—CCH₃ F F	−1.34 $J = 23$ Hzᵃ	−3.10(d) $J = 11$ Hz	Complex mixtureᵇ

ᵃ This spectrum is that of an A₃A₃′XX′ system; the "coupling constant" represents the distance between the major spikes of the absorption. ᵇ See Experimental Section.

Table II. Chemical Shift Differences in Tetramethylethylene Halonium Ions and Their Covalent Precursors

Compound	δ, ppm — Covalent precursor	δ, ppm — Ion	Δδ, ppm
CH₃ CH₃ / CH₃ CH₃ (F F)	−1.34	−3.10	−1.76
CH₃ CH₃ / CH₃ CH₃ (Cl F)	−1.57	−2.72	−1.15
CH₃ CH₃ / CH₃ CH₃ (Br F)	−1.78	−2.86	−1.08
CH₃ CH₃ / CH₃ CH₃ (I F)	−2.00	−3.05	−1.05
CH₃ CH₃ / CH₃ CH₃ (Cl Cl)	−1.77	−2.72	−0.95
CH₃ CH₃ / CH₃ CH₃ (Br Br)	−2.00	−2.86	−0.86
CH₃ CH₃ / CH₃ CH₃ (I I)	−2.30 (estimated)	−3.05	−0.75
CH₃ CH₃ / CH₃ CH₃ (H₃C CH₃)	−0.87	−2.90	−2.03
CH₃ CH₃ / CH₃ CH₃ (H H)	−0.85	−3.32	−2.47

Table II it is apparent that the expected I > Br > Cl trend in ability to bear positive charge is observed.[17] We believe that the experimental data are consistent with bridged halonium ions and not with rapidly equilibrating β-halocarbonium ions. In support of this suggestion we find no change in the spectra of the chloronium, bromonium, or iodonium ions down to −95° in sulfur dioxide–antimony pentafluoride solution. Using sulfuryl chlorofluoride as solvent we were able to attain −130° with the bromonium ion and −120° with the chloronium ion with no change in the spectrum other than slight viscosity broadening and modest, solvent-induced change in position of the absorption. Figures 1 and 2 show the pmr spectra of the tetramethylethylene-chloronium and -bromonium ions in SbF₅–SO₂ solution at −60°.

2,2-Dichloro-3,3-dimethylbutane (pinacolone dichloride) ionizes in antimony pentafluoride–sulfur dioxide solution at −60° to give the bridged tetra-
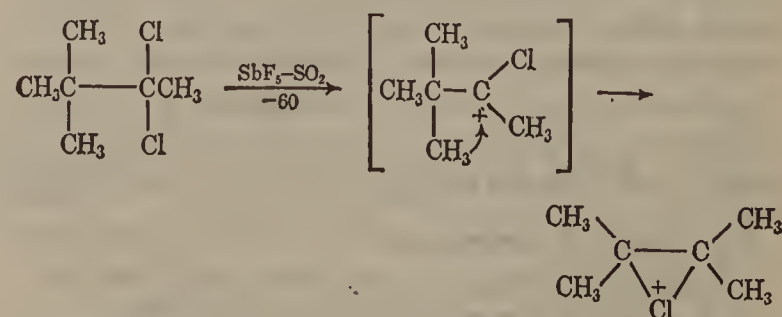
(17) Due to the instability of 2,3-diiodo-2,3-dimethylbutane, the methyl shift could only be calculated for this compound.
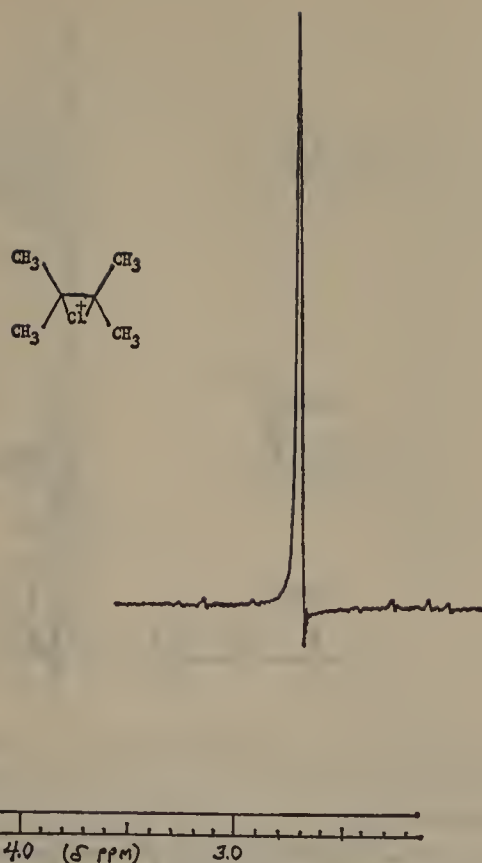
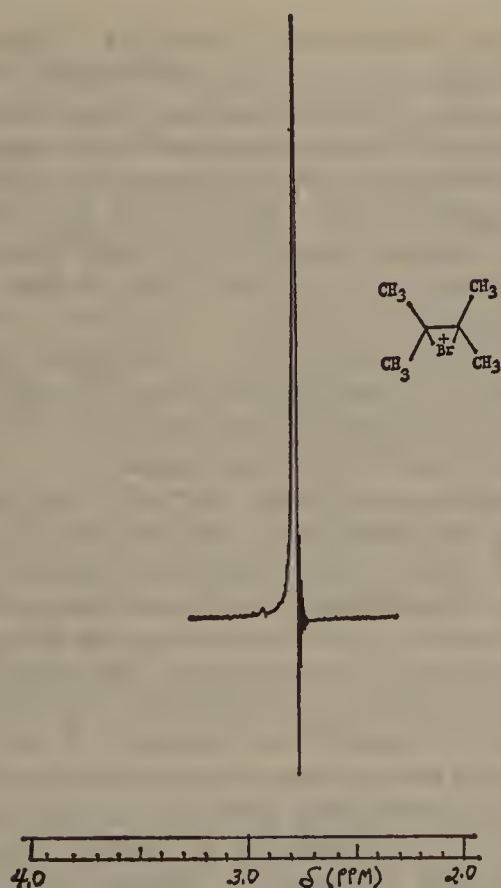Figure 1. Tetramethylethylenechloronium ion in SbF$_5$–SO$_2$ solution at −60°.

Figure 2. Tetramethylethylenebromonium ion in SbF$_5$–SO$_2$ solution at −60°.

Figure 3. Equilibrating dimethylfluoroisopropylcarbonium ion in SbF$_5$–SO$_2$ solution at −90°.

methylethylenechloronium ion. Rapid rearrangement (*via* 1,2-methyl shift) of the intermediate unstable methyl-*t*-butylchlorocarbonium ion with simultaneous strong halogen participation to form the bridged chloronium ion must be assumed.

Further support for the bridged nature of the chloronium, bromonium, and iodonium ions is derived from the contrasting behavior of the fluorinated species,
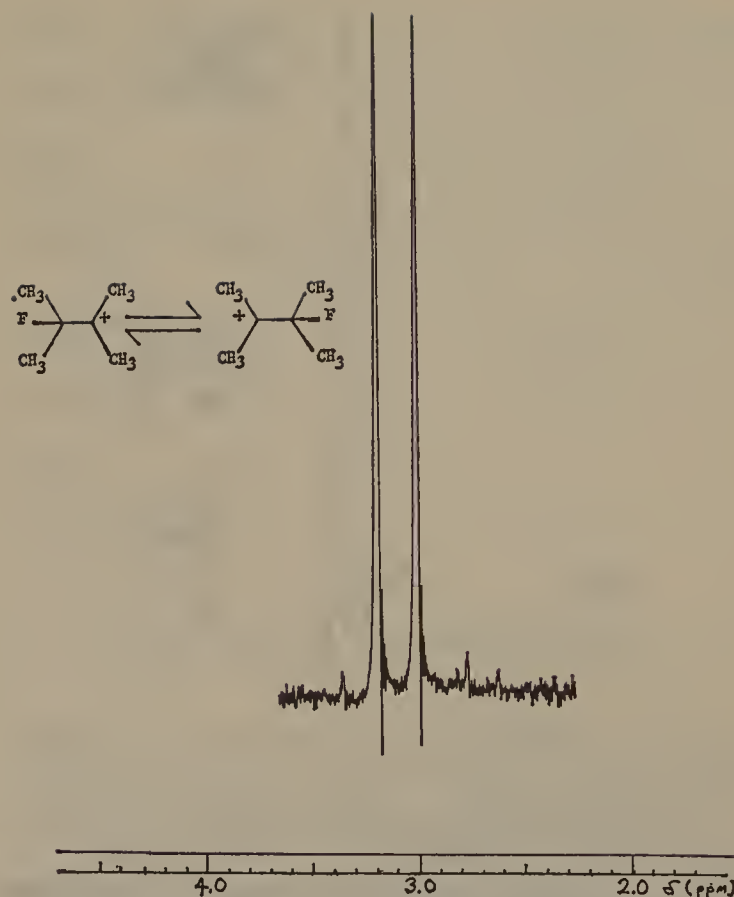
where additional information can be obtained, specifically, spin–spin coupling and direct measurement of a chemical shift for the halogen atom (Figure 3).

From Table II it is evident that the deshielding effect on methyl groups is greatest for the fluorinated ion. This is expected on the basis of electronegativity, but since the deshielding (1.76 ppm) is nearly twice that of the chloronium ion (0.95 ppm) we suggest that a change in behavior is indicated, *i.e.*, *a change from a static bridged species to equilibrating β-fluorocarbonium ions*. In Table II, we have included Δδ's for the pentamethylethyl cation which is not bridged, since it shows, even at −170°, only one kind of methyl group,[18] and the dimethylisopropylcarbonium ion, which also is a rapidly equilibrating but not bridged ion.[18] These equilibrating ions have Δδ's falling in the same general order of magnitude as the dimethyl-α-fluoroisopropylcarbonium ion.

Strong support for the equilibrating β-fluorocarbonium ion is also found in the chemical shift of the fluorine atom. Initially, difficulty was experienced in locating the fluorine spectrum because of the high degree of coupling. The fluorine resonance was located by heteronuclear spin–spin decoupling, *i.e.*, by observing the proton spectrum while irradiating the fluorine region. (We used benzyl fluoride to correlate the positions of the fluorine resonance with the decoupling frequency.) The fluorine in the carbonium ion is found at about +119 ppm, only 31 ppm downfield from the starting difluoride (ϕ = +150 ppm in CCl$_4$ from external CCl$_3$F). This is the region where antimony–fluorine resonances are observed so that in our solvent systems we could not directly determine the chemical shift for this fluorine atom. It is quite clear, however,

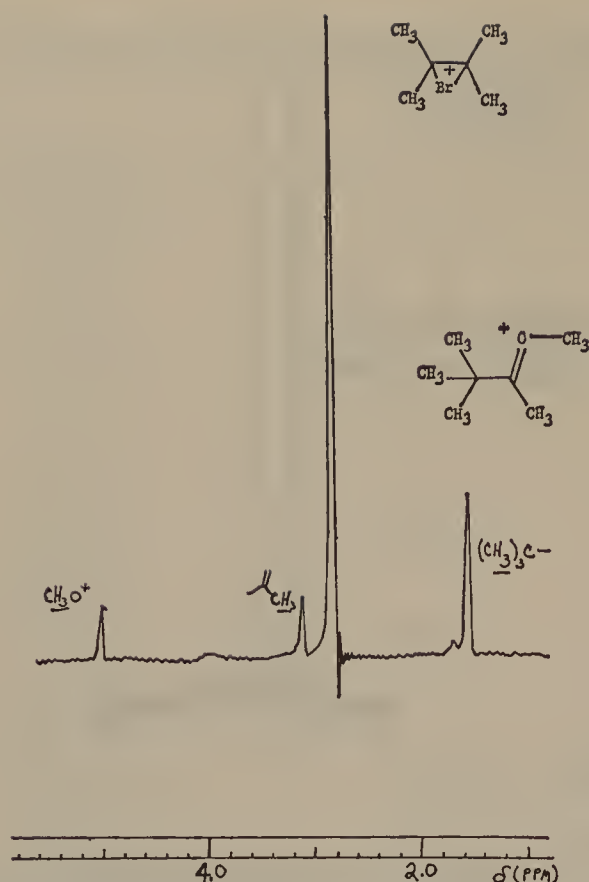(18) G. A. Olah and J. Lukas, *J. Am. Chem. Soc.*, 89, 4739 (1967).

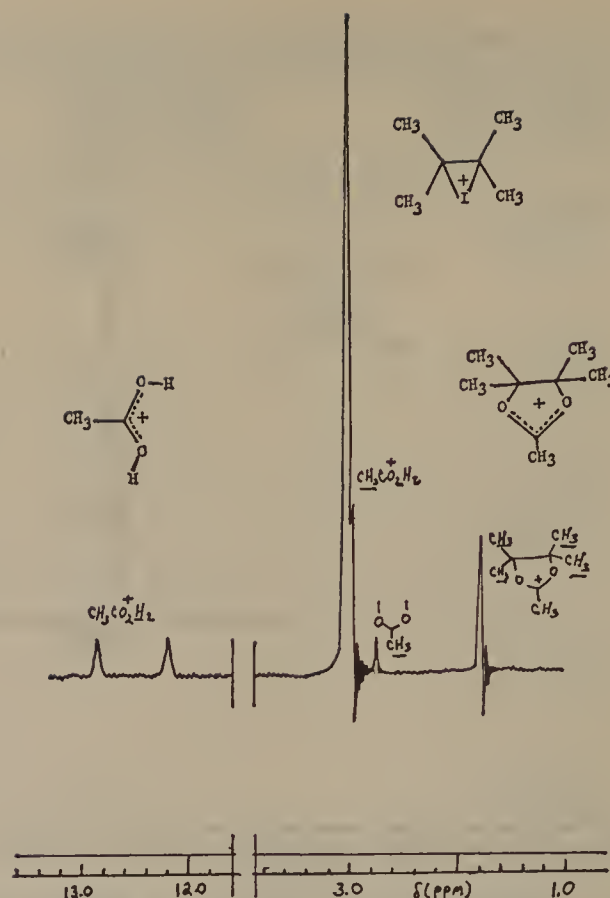Figure 4. Ionization of 2-bromo-3-methoxy-2,3-dimethylbutane in FSO₃H–SbF₅–SO₂ solution at −60°.

Figure 5. Ionization of 2-iodo-3-acetoxy-2,3-dimethylbutane in FSO₃H–SbF₅–SO₂ solution at −60°.

that the fluorine resonance appears in the region expected for a fluorine atom β to a positively charged carbon atom[19] and quite far from the region expected for fluorine on a positive carbon atom.[20] We suggest also that this shift is inconsistent with that expected for a bridged fluorine ion, where at least partial positive charge would be expected on fluorine. The measured spin–spin coupling of $J_{H-F} = 11$ Hz is consistent with equilibrating ions where one would expect an average of the three-bond coupling (21–22 Hz), and the four-bond coupling (1.2 Hz). It is, of course not obvious what one should expect for the coupling in a bridged fluoronium ion.[21]

We attempted to freeze out the two different kinds of methyl groups, but this did not occur even at −95°. Poor solubility prevented us from attaining lower temperatures.

We also examined the ionization of 2-halo-2-methoxy- and 2-halo-3-acetoxy-2,3-dimethylbutanes in both antimony pentafluoride–sulfur dioxide and in antimony pentafluoride–fluorosulfonic acid–sulfur dioxide solution. Besides the bridged halonium ions we obtained bridged acetoxonium ions, examples of which are well known,[22] but not bridged ethyleneoxonium ions.[23] The

(19) G. A. Olah and C. U. Pittman, Jr., J. Am. Chem. Soc., 88, 3310 (1966), report $\Delta\phi = -24.8$ ppm for (CF₃)CH₃C⁺C₆H₅ (compared with the covalent precursors) in FSO₃H–SbF₅–SO₂ solution, which compares favorably with $\Delta\phi = -31$ ppm observed in this work.

(20) G. A. Olah, M. B. Comisarow, and R. D. Chambers, ibid., 89, 1268 (1967), report a chemical shift of $\phi = -182.0$ ppm for CH₃-C⁺FCH₃. This rules out rapid scrambling of methyl groups as in (CH₃)₃CC⁺FCH₃.

(21) We intuitively feel that the coupling constant would be considerably larger for a cyclic species. We know of no pertinent evidence to cite.

(22) H. Hart and D. Tomalia, Tetrahedron Letters, 3383, 3389 (1966); C. B Anderson, E. C. Liedluch, and S. Winstein, ibid., 2037 (1963); H. Meerwein, V. Hederick, V. Morschel, and K. Wunderlich, Ann., 635, 1 (1960), and references therein.

(23) This is not unexpected, since this group is known to cause rate decreases rather than rate enhancements in the β position.

pmr data are summarized in Table III. Figures 4 and 5 show representative examples of the spectra.

Interestingly, 2-chloro-2-acetoxy-2,3-dimethylbutane in FSO₃H–SbF₅–SO₂ solution gave 95% bridged acetate, whereas the iodo and bromo derivatives gave 80–90% bridged halonium ion. Methoxy is a good leaving group in antimony pentafluoride–sulfur dioxide solution as evidenced by the formation of high yields of tetramethylethylenehalonium ions from 1-halo-2-methoxy-2,3-dimethylbutanes. Protonated methanol[24] and protonated acetic acid[25] formed through protonation of the leaving groups are stable in the acid system and were known from previous work.

The quenching of all ions with cold methanol in the presence of potassium carbonate was straightforward in every case except that of the ion formed from 2,3-difluoro-2,3-dimethylbutane, giving high yields of the expected methoxy derivatives. In the latter case, a mixture consisting of pinacolone, 2-fluoro-2-methoxy-2,3-dimethylbutene-1, and 2-methoxy-2,3-dimethylbutene-1 (major product) was obtained. It seemed possible that the elimination occurred in work-up because of the excess carbonate, and so a second quench was performed in the presence of sodium bicarbonate. Again the same mixture was obtained, but now pinacolone was the major product. In both cases, there were several unidentified components present in small amounts. We have not rationalized the behavior of this ion, but it is another example of the contrasting behavior exhibited by the fluorine member of the series. The solutions of ions obtained by ionization of oxygenated precursors were not quenched since they invariably contained a mixture of species.

(24) G. A. Olah and E. Namanworth, J. Am. Chem. Soc., 88, 5327 (1966); G. A. Olah, J. Sommer, and E. Namanworth, ibid., 89, 3576 (1967).

(25) G. A. Olah and A. M. White, ibid., 89, 3591 (1967).
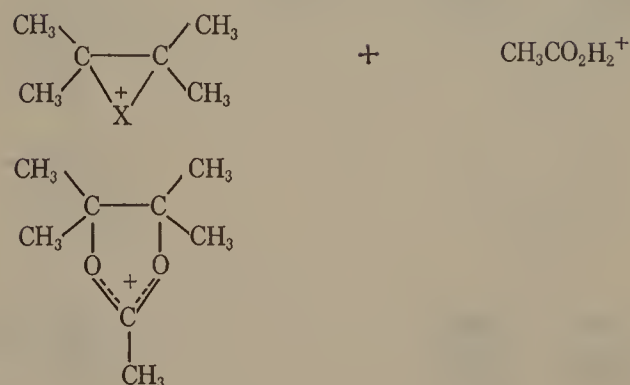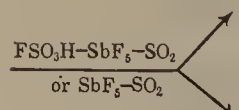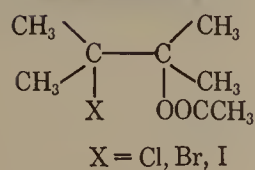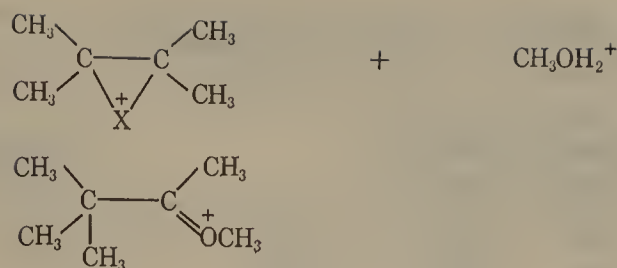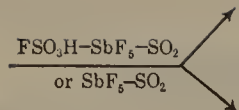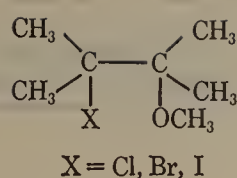
Finally, it should be mentioned that in contrast to other members of this series, the β-fluorocarbonium ion completely decomposes at Dry Ice temperature in antimony pentafluoride–sulfur dioxide solution within a week. The tetramethylenehalonium ions under similar conditions are stable for long periods of time (no decomposition was noted after several weeks at $-78°$).

Experimental Section

Preparation of Ions. Solutions of the ions were obtained in the following way. A saturated solution of antimony pentafluoride in sulfur dioxide was prepared (at $-10°$). Two-milliliter portions of this solution were cooled to $-78°$, causing some antimony pentafluoride to crystallize from solution. To this suspension was added dropwise with stirring approximately 0.3 g of the appropriate dihalide (methoxy-, acetoxy halide). Slight warming was required to complete the ionization, whereupon a homogeneous solution resulted with only slight traces of color. Ion concentrations were approximately 10%. These operations were carried out in the laboratory atmosphere. This procedure provides a simple way to generate carbonium ions in a highly reproducible manner.

Solutions of the ions in $FSO_3H–SbF_5–SO_2$ solutions were prepared in the following way. Approximately 1.5 ml of $HSO_3F–SbF_5$ (1:1 M solution) in an equal volume of sulfur dioxide was cooled to $-78°$. The precursor (approximately 0.2 ml) was dissolved in 1 ml of sulfur dioxide, cooled to $-78°$, and with vigorous agitation, slowly added to the acid solution.

Very low temperature spectra (-130 to $-100°$) were obtained in sulfuryl chlorofluoride (Allied Chemical) solution. In this solvent, solubility of the ions was generally less than in sulfur dioxide, and solid material, if present in the samples, was removed by centrifuging.

Spectra were recorded either on a Varian Model A-56-60A spectrometer with external TMS in deuteriochloroform as reference (0.5 ppm has been added to these chemical shifts to correct them to TMS in a capillary as reference) or on a Varian Model HA-60 spectrometer with TMS in a capillary as reference. The nmr spectrometers were equipped with low-temperature probes (on the HA-60 model we used a special low-temperature probe enabling work down to $-180°$).

The fluorine-decoupling experiment was performed, using an NMR Specialties Model SD-60B spin–spin decoupler to generate the 56.4-MHz signal. Integrated areas were consistent with assigned structures.

Methanolysis of the ions was accomplished by adding slowly the solution of the carbonium ion in sulfur dioxide to a suspension of methanol and potassium carbonate at $-78°$. Product isolation was accomplished by drowning the resulting suspension in water and extracting with pentane. Identification of products was made by glpc comparison of retention times with authentic samples and by nmr and infrared spectroscopy.

Preparation of 2-Chloro-3-fluoro-2,3-dimethylbutane. To a solution of 25 g of anhydrous hydrogen fluoride and 50 ml of dry ether were alternately added, at $-78°$, 4.2 g (0.05 mole) of tetramethylethylene (Aldrich) and 5.6 g (0.051 mole) of t-butyl hypochlorite (Frinton Laboratories) over a period of 5 min. The reaction mixture was stirred for 1 hr at $-78°$ and an additional 1 hr at $0°$, and then poured into ice water containing excess potassium carbonate. An additional 60 ml of ether was added, and the layers separated. Removal of solvent left an oil, which after flash distillation at 1 mm partially crystallized. The yield was 3.6 g, 46% of material containing small amounts of an unknown contaminant. The analytical sample was purified by preparative gas chromatography on an Apiezon L on Chromosorb W column. It had mp 63–64°.

Anal. Calcd for $C_6H_{12}ClF$: C, 51.99; H, 8.73; Cl, 25.57; F, 13.70. Found: C, 52.25; H, 8.81; Cl, 25.69; F, 13.25.

Preparation of 2-Bromo-3-fluoro-2,3-dimethylbutane. This material was prepared by the procedure of Kent and Freeman.[26] From 25.2 g (0.3 mole) of tetramethylethylene and 53.4 g (0.3 mole) of N-bromosuccinide in 70 g of anhhydrous hydrogen fluoride diluted with 140 ml of dry ether, there was obtained 33.0 g of compound, 60%, mp 85–87°, after sublimation. The analytical sample was prepared by recrystallization from hexane followed by sublimation and had mp 87–89°.

Anal. Calcd for $C_6H_{12}BrF$: C, 39.36; H, 6.61; Br, 43.65; F, 10.38. Found: C, 39.60; H, 6.68; Br, 43.38; F, 10.62.

Preparation of 2-Fluoro-3-iodo-2,3-dimethylbutane. This compound was prepared by the method of Wood, Kent, and Fisher.[27] From 8.4 g (0.1 mole) of tetramethylethylene and 22.5 g (0.1 mole) of N-iodosuccinimide in 20 g of anhydrous hydrogen fluoride diluted with 100 ml of anhydrous ether, there was obtained 12.7 g, 55% of material, mp 63–65° after sublimation. This compound decomposed readily and was not analyzed.

Preparation of 2,3-Difluoro-2,3-dimethylbutane. 2-Bromo-3-fluoro-2,3-dimethylbutane (33 g, 0.18 mole) was dissolved in 150 ml of anhydrous acetonitrile. To this solution, cooled to $-20°$ (Dry Ice–carbon tetrachloride), was added in portions with stirring 63.5 g (0.5 mole) of silver fluoride (argentous, Harshaw) over a 10-min period. The solution was stirred 4 hr at $-20°$ and then for 24 hr at $0°$. The reaction mixture was filtered and poured into ice water. The organic layer was washed ten times with 50-ml portions of ice water and dried over sodium sulfate. The reaction mixture was flash distilled at about 10 mm (no heating) which allowed the recovery of 9.5 g of starting material. The more volatile components of the mixture consisted of the desired 2,3-difluoro-2,3-dimethylbutane, isolated yield (by preparative vpc, Apiezon L on Chromosorb W column) 1.2 g, 5%, 3-fluoro-2,3-dimethylbutene, 43%, and unreacted starting material. (The yields are based on total starting material.) The separation of the reaction mixture was unsuccessful due to decomposition with attempted distillation

(26) P. W. Kent and M. R. Freeman, *J. Chem. Soc.*, 912 (1966); P. W. Kent, F. O. Robson, and V. A. Welch, *ibid.*, 3273 (1963); P. W. Kent and J. E. G. Barnett, *ibid.*, 6196 (1964).

(27) K. R. Wood, P. W. Kent, and D. Fisher, *ibid.*, 912 (1966).

Table III. Pmr Data of 2-Halo-3-methoxy- (-acetoxy-) 2,3-dimethylbutanes and Their Ions in FSO_3H–SbF_5–SO_2 and SbF_5–SO_2 Solutions

2-Halo-3-methoxy-(-acetoxy-) 2,3-dimethylbutane, intern. TMS in CCl_4[a]	Ion in SbF_5–FSO_3H–SO_2, extern. TMS in $DCCl_3$	Ion in SbF_5–SO_2, extern. TMS in $DCCl_3$
(structure: $(CH_3)_2C(Cl)–C(OCH_3)(CH_3)_2$) −1.16(d) $J = 1.1$ Hz; −1.28(d) $J = 2.2$ Hz; −3.22(d) $J = 1.1$ Hz	$CH_3\overset{+}{O}H_2$ [c] −4.50(t) $J = 3.9$ Hz; −9.72(q) $J = 1.0$ Hz. (allyl cation structure)[b] −2.46(d); −3.50(m); −3.58(m); −7.90(m); −8.46(m). 95%	Same ions in slightly different amounts
	(oxocarbenium structure $CH_3C=\overset{+}{C}(OCH_3)$) −1.46(s); −3.02(s); −4.94(s). 5%	
(structure: $(CH_3)_2C(Cl)–C(OCH_3)(CH_3)_2$) −1.28(s); −1.52(s); −3.20(s)	(allyl cation structure) (minor amount)	(chlorinated cation structure $(CH_3)_2C(Cl)^+C(CH_3)_2$) 75%
	$CH_3\overset{+}{O}H_2$ (major)	(oxocarbenium structure CH_3O^+) 25%
	(chloronium structure $(CH_3)_2\overset{+}{C}lC(CH_3)_2$) −2.69(s)	Traces of $CH_3O^+H_2$
		(allyl cation structure)
(structure: $(CH_3)_2C(Br)–C(OCH_3)(CH_3)_2$) −1.35(s); −1.80(s); −3.24(s)	$CH_3\overset{+}{O}H_2$. (bromonium structure $(CH_3)_2\overset{+}{B}rC(CH_3)_2$) −2.76(s)	(bromonium structure $(CH_3)_2\overset{+}{B}rC(CH_3)_2$) 50%
	(oxocarbenium structure $CH_3C=\overset{+}{C}(OCH_3)$) Trace	(oxocarbenium structure CH_3O^+) 50%
(structure: $CH_3C(I)(CH_3)–C(OCH_3)(CH_3)CH_3$) −1.37(s); −1.84(s); −3.26(s)	(oxocarbenium structure $CH_3C=\overset{+}{C}(OCH_3)$) 55%	(iodonium structure $(CH_3)_2\overset{+}{I}C(CH_3)_2$) 90%
	(iodonium structure $(CH_3)_2\overset{+}{I}C(CH_3)_2$) 45%. $CH_3\overset{+}{O}H_2$. 3.00(s)	(oxocarbenium structure $CH_3C=\overset{+}{C}(OCH_3)$) 10%
(structure: $CH_3C(OCH_3)(CH_3)–C(OCH_3)(CH_3)CH_3$) −1.15(s); −3.18(s)	(oxocarbenium structure $CH_3C=\overset{+}{C}(OCH_3)$)	Same
(structure: $CH_3C(Cl)(CH_3)–C(OCH_3)(CH_3)CH_3$) −1.57(s); −1.62(s); −1.92(s)	(acetoxonium structure $(CH_3)_2C–O\overset{+}{–}O–C(CH_3)_2$, CH_3) −1.90(s); −2.84(s)	(acetoxonium structure) 95%
	(chloronium structure $(CH_3)_2\overset{+}{C}lC(CH_3)_2$) Trace	(chloronium structure $(CH_3)_2\overset{+}{C}lC(CH_3)_2$) 5%

Table III *continued*

2-Halo-3-methoxy- (-acetoxy-) 2,3-dimethylbutane, intern. TMS in CCl₄[a]	δ, ppm	
	Ion in SbF₃–FSO₃H–SO₂, extern. TMS in DCCl₃	Ion in SbF₅–SO₂, extern. TMS in DCCl₃

H₃C CH₃ / CH₃C–CCH₃ / Br OCH₃ —1.70(s) —1.82(s) —1.96(s)

CH₃C(OH)(OH)⁺

Br-bridged ion 90% / acetoxonium ion 10% (SbF₃–FSO₃H–SO₂)

Br-bridged ion 70% / acetoxonium ion 30% (SbF₅–SO₂)

CH₃ₐ, CH₃ᵦ a —1.99(s)
CH₃ₐ | CH₃ᵦ b —1.69(s)
  I OCH₃c c —2.01(s)

CH₃C(OH)(OH)⁺

I-bridged ion 85% / acetoxonium ion 15% (SbF₃–FSO₃H–SO₂)

I-bridged ion 90% / acetoxonium ion 10% (SbF₅–SO₂)

CH₃C(OH)(OH)⁺

[a] Abbreviations used are: d, doublet; s, singlet; m, multiplet; t, triplet; and q, quadruplet. [b] The dimethylisopropenylcarbonium ion (1,1-dimethyl-2-methylallyl cation) exhibits a temperature-dependent spectrum indicating an observable rotational barrier. We will report in a forthcoming communication in detail on this ion. [c] See ref 24.

through a short-packed column. The fluoroolefin was unstable and had to be stored over anhydrous potassium carbonate. It could not be protonated to give a stable carbonium ion.

Anal. Calcd for C₆H₁₂F₂: C, 58.99; H, 9.90; F, 31.10. Found: C, 58.93; H, 9.40; F, 31.00.

Preparation of 2-Chloro-3-methoxy-2,3-dimethylbutane. To 30 ml of methanol containing 0.2 ml of concentrated sulfuric acid were alternately added, in small portions, 4.2 g of tetramethylethylene (0.05 mole) and 5.5 g (0.05 mole) of *t*-butyl hypochlorite. The reaction caused the solution to warm considerably and ice-bath cooling was applied to maintain room temperature. The reaction mixture was then poured into 100 ml of water and extracted with 75 ml of pentane. Removal of solvent left an oil which was flash distilled under vacuum. The yield was 6.0 g, 40%. The analytical sample was purified by preparative vpc and had mp 43–45°.

Anal. Calcd for C₇H₁₅ClO: C, 55.81; H, 10.04; Cl, 23.53; O, 10.62. Found: C, 55.75; H, 10.02; Cl, 23.39; O, 10.84.

Preparation of 2-Bromo-3-methoxy-2,3-dimethylbutane. To 30 ml of methanol containing 0.2 ml of concentrated sulfuric acid were alternately added in portions 4.2 g (0.05 mole) of tetramethylethylene and 8.9 g (0.05 mole) of N-bromosuccinimide. The reaction was exothermic and ice-bath cooling was required to maintain the temperature at 25°. After pouring the reaction mixture into 100 ml of water and extracting with 75 ml of pentane, there was obtained 5.7 g (58%) of the desired compound. The analytical sample was prepared by preparative vpc and had mp 90–92°. The crude product was oily and could not be induced to crystallize even after flash distillation.

Anal. Calcd for C₇H₁₅BrO: C, 43.09; H, 7.75; Br, 40.96; O, 8.20. Found: C, 43.02; H, 7.56; Br, 40.73; O, 8.69.

Preparation of 2-Iodo-3-methoxy-2,3-dimethylbutane. This compound was prepared in the same way as the two previous halo ethers except that the temperature was maintained at 0°. The yield from 0.05 mole of tetramethylethylene and N-iodosuccinimide

was 6.5 g, 54%, of white crystalline solid which rapidly decomposed at room temperature. No melting point or analysis could be obtained. The low-temperature pmr spectrum was completely consistent with the assigned structure. The crystalline material could be stored indefinitely at −78°.

Preparation of 2-Fluoro-3-methoxy-2,3-dimethylbutane. To 19.5 g (0.1 mole) of 2-bromo-3-methoxy-2,3-dimethylbutane in 100 ml of anhydrous acetonitrile at 0° was added 38.1 g (0.3 mole) of silver fluoride. The reaction mixture was allowed to warm to room temperature and then stirred for 4 hr. Filtration of the mixture allowed removal of excess silver fluoride and precipitated silver bromide. The filtrate was poured into 200 ml of cold water, extracted with 100 ml of pentane, and then washed twice with 50-ml portions of cold water. Pentane was removed by distillation and the remaining oil was separated into its components by preparative vpc at 100°. There were four major components, the first of which was pinacolone, 35%, identified by its vpc retention time and pmr spectrum; the second was 3-methoxy-2,3-dimethylbutene-1 (pmr spectrum in CCl₄: δ 0.97 (s), δ 1.68 (m), δ 2.99 (s), and δ 4.83 (m), amounting to 35%; the third was the desired 2-fluoro-3-methoxy-2,3-dimethylbutane and amounted to 20%; a fourth component was unreacted starting material, 10%.

Anal. Calcd for C₇H₁₅FO: C, 62.65; H, 11.27; F, 14.16; O, 11.92. Found: C, 62.82; H, 11.16; F, 14.39; O, 11.63.

Preparation of 2-Chloro-3-acetoxy-2,3-dimethylbutane. To 30 ml of glacial acetic acid containing 4.2 g (0.05 mole) of tetramethylene was added dropwise with stirring 5.5 g (0.05 mole) of *t*-butylhypochlorite over a period of 15 min. Ice-bath cooling was required to keep the temperature near that of room temperature. The reaction mixture was poured into 100 ml of cold water and extracted with 100 ml of pentane. Solvent removal left an oil which was flash distilled to yield 5.3 g, 60%, of the desired compound. The analytical sample was purified by preparative vpc.

Anal. Calcd for C₈H₁₅ClO: C, 53.78; H, 8.46; Cl, 19.84; O, 17.91. Found: C, 54.00; H, 8.59; Cl, 20.08; O, 17.33.

Preparation of 2-Bromo-3-acetoxy-2,3-dimethylbutane. This compound was prepared in the same way as the chloro derivative using N-bromosuccinimide. From 0.05 mole of reagents there was obtained 8.6 g, 77%, of compound, bp 73–77° (9 mm). The analytical sample was a center cut, bp 74°.

Anal. Calcd for $C_8H_{15}BrO$: C, 43.07; H, 6.77; Br, 35.81; O, 14.34. Found: C, 43.31; H, 6.93; Br, 35.36; O, 14.40.

Preparation of 2-Iodo-3-acetoxy-2,3-dimethylbutane. This compound was prepared in the same way as the bromo derivative using N-iodosuccinimide and maintaining the temperature at 0°. From 0.05 mole of reagents there was obtained 7.6 g, 50%, of desired compound. This material was unstable and had to be stored at −78°. It could be stabilized with sodium sulfite. Attempted purification by vacuum distillation resulted in decomposition. This material was used without purification. The absence of appreciable extraneous absorptions in its pmr spectrum indicates better than 90% purity.

Stable Carbonium Ions. XLIX.[1] Protonated Dicarboxylic Acids and Anhydrides and Their Cleavage to Oxocarbonium Ions

George A. Olah and Anthony M. White[2]

Contribution from the Department of Chemistry, Case Western Reserve University, Cleveland, Ohio 44106. Received April 21, 1967

Abstract: A series of diprotonated aliphatic dicarboxylic acids (alkylenedicarboxonium ions) have been studied in HSO_3F–SbF_5–SO_2 solution. O-diprotonation was observed with negligible exchange rates at low temperature by nmr spectroscopy. Glutaric, adipic, and pimelic acids were found to cleave at higher temperatures, first to the alkylenemonooxocarbonium–monocarboxonium ions, and then to the alkylenedioxocarbonium ions. Only the monooxocarbonium ion was observed in the case of succinic acid. Protonated oxalic and malonic acids did not cleave in the acid system. Protonation of dicarboxylic acid anhydrides in FSO_3H–SbF_5–SO_2 solution, even at −90°, leads to a mixture of the corresponding monocarboxonium–monooxocarbonium ion.

The isolation of alkylenedioxocarbonium ion salts from dicarboxylic acid fluorides and antimony pentafluoride has been reported recently.[3] In continuation of our previous work on the observation of the formation of oxocarbonium ions from protonated aliphatic carboxylic acids in FSO_3H–SbF_5,[4] we now report the formation of dioxocarbonium ions from protonated aliphatic dicarboxylic acids.

Results and Discussion

The ionization of saturated dicarboxylic acids in sulfuric acids has been investigated by cryoscopy,[5] and it was concluded that succinic acid and higher members of the series are only partially ionized as diacid bases ($i = 2.6$). Malonic acid was reported to be only monoprotonated ($i = 2.0$) and oxalic acid gave an i factor of 1.3 which increased with time due to decomposition. Pittman[6] has studied the change in nmr band positions of adipic acid in H_2SO_4–oleum and found a downfield shift in the α-proton signal in 17% oleum, but was unable to assign the species under observation on the available evidence.

In the strong acid system, FSO_3H–SbF_5, all the aliphatic dicarboxylic acids studied were completely diprotonated, and we were able to observe, in certain cases, cleavage to the corresponding monocarboxonium–monooxocarbonium ion and dioxocarbonium ions.

$$HO_2C(CH_2)_nCO_2H \xrightarrow[-60°]{FSO_3H–SbF_5–SO_2}$$

$$H_2\overset{+}{O}_2C(CH_2)_n\overset{+}{C}O_2H_2 \xrightarrow[\Delta(-H_2O)]{FSO_3H–SbF_5–SO_2}$$

$$H_2\overset{+}{O}_2C(CH_2)_n\overset{+}{C}O \xrightarrow[\Delta(-H_2O)]{FSO_3H–SbF_5–SO_2} \overset{+}{O}C(CH_2)_n\overset{+}{C}O$$
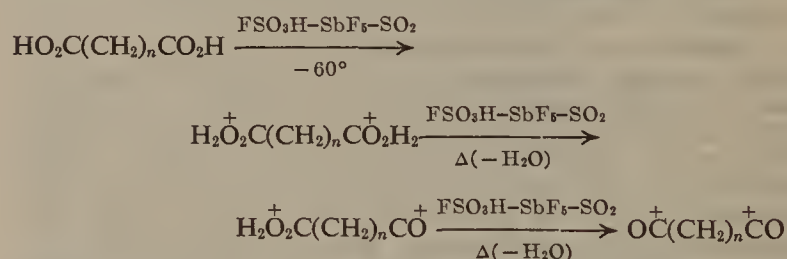
The following aliphatic dicarboxylic acids were examined in FSO_3H–SbF_5–SO_2 solution: oxalic, malonic, glutaric, adipic, and pimelic acids.

Diprotonated Dicarboxylic Acids (Alkylenedicarboxonium Ions). Dicarboxylic acids, with the exception of oxalic acid, gave well-resolved nmr spectra in FSO_3H–SbF_5 solution diluted with SO_2. To observe the protons on oxygen, it was necessary to record the spectra, in general, at lower temperatures (−90°) than in the case of the monocarboxylic acids[3] because of the more weakly basic nature of the diacids. At these low temperatures, the C–H protons sometimes show broadening, and the coupling constants between methylene protons were evaluated from spectra recorded at −40°. Table I summarizes the coupling constants and chemical shifts. Representative spectra are given in Figures 1–4. Integration of the peaks indicated four protons

(1) Part XLVIII: G. A. Olah and J. M. Bollinger, *J. Am. Chem. Soc.*, **89**, 4744 (1967).
(2) National Institutes of Health Postdoctoral Research Investigator, 1966–1967.
(3) G. A. Olah and M. B. Comisarow, *J. Am. Chem. Soc.*, **88**, 3313 (1966).
(4) G. A. Olah and A. M. White, *ibid.*, **89**, 3591 (1967).
(5) A. Wiles, *J. Chem. Soc.*, 996 (1953).
(6) C. U. Pittman, Jr., Ph.D. Thesis, The Pennsylvania State University, 1964.

$H_2O_2\overset{+}{C}-CH_2CH_2\overset{+}{C}O_2H_2$

Figure 1.

$H_2O_2\overset{+}{C}-CH_2CH_2CH_2\overset{+}{C}O_2H_2$

Figure 2.

$H_2O_2\overset{+}{C}-CH_2(CH_2)_2CH_2\overset{+}{C}O_2H_2$
$\quad\quad\quad\alpha\quad\quad\quad\beta$

Figure 3.

$H_2O_2\overset{+}{C}-(CH_2)_5\overset{+}{C}O_2H_2$
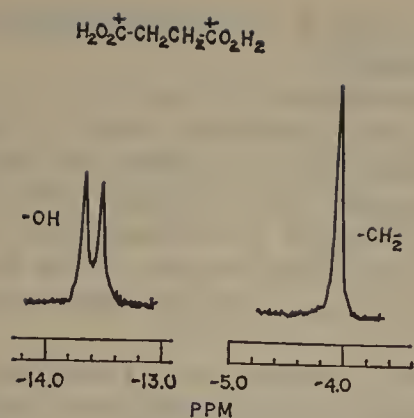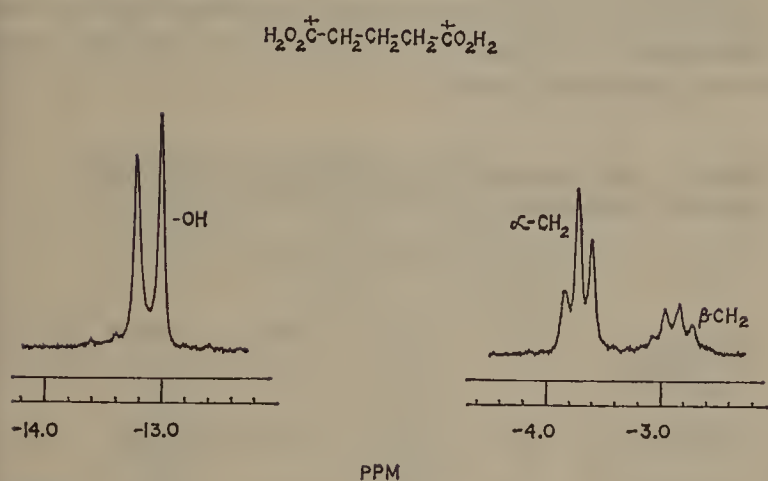
Figure 4.

on oxygen. This shows that all investigated dicarboxylic acids exist in the acid solution as diprotonated species.

$$(CH_2)_n(CO_2H)_2 \xrightarrow{\text{FSO}_3\text{H–SbF}_5\text{–SO}_2} (CH_2)_n(CO_2H_2)^{2+}$$
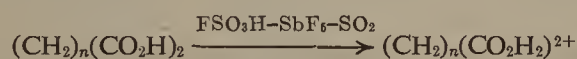
Table I. Nmr Chemical Shifts (in ppm)[a] and Coupling Constants (in Hz) of Protonated Dicarboxylic Acids (Alkylenedicarboxonium Ions)

Acid	Temp, °C	OH	CH₂
(COOH)₂	−90	−15.70	
(CH₂)(COOH)₂	−90	−14.60	−5.23
(CH₂)₂(COOH)₂	−70	−13.68	−4.08
		−13.52	
(CH₂)₃(COOH)₂	−70	−13.25	−3.70[a]
		−13.05	−2.87[b]
(CH₂)₄(COOH)₂	−60	−12.98	−3.53[b]
		−12.72	−2.35[c]
(CH₂)₅(COOH)₂	−60	−12.77	−3.43[b]
		−12.50	−2.08[d]

[a] Referred to external TMS. [b] Triplet, $J = 7$ Hz. [c] Pentuplet, $J = 7$ Hz. [d] Multiplet.

In the case of oxalic acid, the large deshielding observed suggested that this acid, too, was diprotonated. At −90° both the protons on oxygen and the acid solvent had nmr signals which were considerably broadened, indicative of exchange. We attempted to confirm that oxalic acid was indeed diprotonated by integration of the –OH⁺ protons against an internal standard (tetramethylammonium hexafluoroantimonate) but found that the low solubility of protonated oxalic acid at −90° prevented us from obtaining reproducible results.
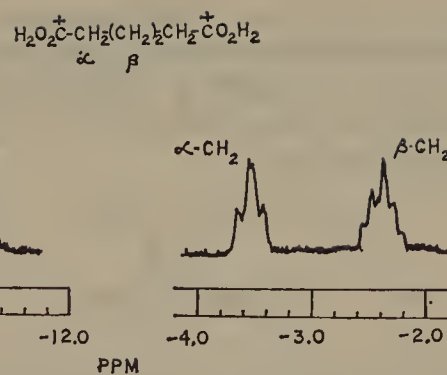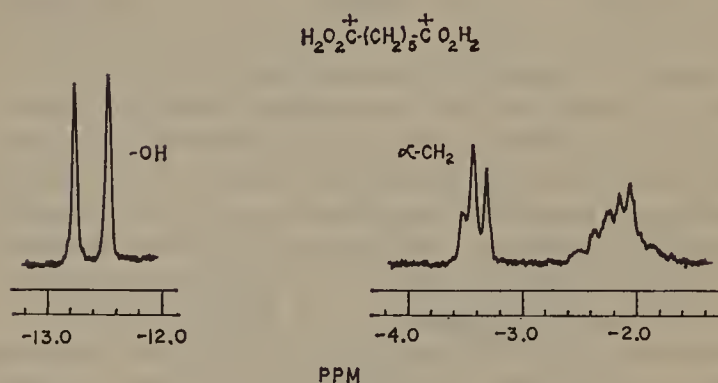
Succinic, glutaric, adipic, and pimelic acids all have two peaks of equal area in the hydroxyl region at low temperature indicating, as in the case of aliphatic monocarboxylic acids, that protonation is occurring on the carbonyl oxygen and that the two protons have nonequivalent environments. This is interpreted, as in the case of protonated monocarboxylic acids,[4] as a consequence of structure I being the predominant species.

I
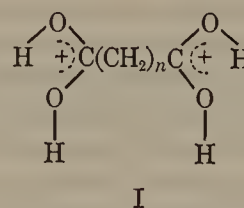
The temperature at which collapse to a single absorption occurs decreased with decreasing separation of the acid functions, and in the case of malonic and oxalic acids, only a single absorption peak was observed at the lowest temperature studied (−90°).

The chemical shift of the OH peaks appears to be very dependent on chain length, and the results suggest a correlation between the basicity of the carbonyl oxygens and the chemical shift of the hydroxyl protons. A similar correlation has been noted in the case of protonated cyclic ketones for which basicity data are available.[7]

Diprotonated "Squaric Acid." 1,2-Dihydroxycyclobutenedione ("squaric acid") is to be considered as a dicarboxylic acid. In many of its reactions[8,9] squaric acid behaves as a strong organic acid because of the resonance stabilization of its dianion. The dication, if squaric acid were diprotonated and the hydroxycarbonium ion was a contributor to the structure,

(7) G. A. Olah and M. Calin, *J. Am. Chem. Soc.*, **89**, 4736 (1967).
(8) G. Maaks and P. Hegenberg, *Angew. Chem. Intern. Ed. Engl.*, **5**, 888 (1966).
(9) D. T. Ireland and H. F. Walton, *J. Phys. Chem.*, **71**, 751 (1967).

would formally be a Hückel aromatic system. The cyclobutenium dication form (II) would be expected to exert a strong stabilizing influence with significant delocalization of the positive charge from the oxygen atoms into the ring.

II
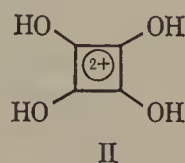
We have found that in all other oxygen-protonated species examined, the chemical shift of the proton on oxygen is a good measure of the distribution of charge in the molecule. Observation of the hydroxyl protons in diprotonated squaric acid should thus provide a measure of the contribution from the dicyclobutenium dication form of the molecule. The only previous report of protonated species from squaric acid is the suggestion that the changes in the ultraviolet absorption spectrum of squaric acid found in acidic media (1 M sulfuric acid) was a result of protonation.[9]

We found that squaric acid in FSO_3H–SbF_5–SO_2 solution at $-90°$ gives a single peak in the nmr spectrum at -14.50 ppm. This large deshielding is comparable with that found in diprotonated malonic acid, and we feel that this result implies that there is no significant contribution of the cyclobutenium dication to the stability of this molecule. We suggest that the predominant resonance forms of diprotonated squaric acid are of the type indicated below.
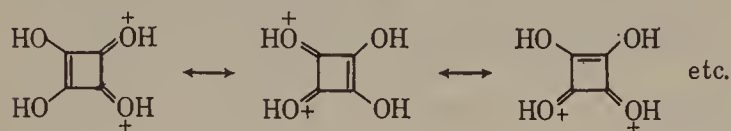
On raising the temperature, exchange with the solvent is observed, as in other protonated dicarboxylic acids. At $-70°$, we observed the appearance of a new peak at -13.67 ppm. This was about 10% of the area of the low-field OH+ peak and disappeared on lowering the temperature again to $-90°$. As yet the identity of this new species has not been established.

Cleavage of Alkylenedicarboxonium Ions to Alkylenemonooxocarbonium–Monocarboxonium Ions. The ease with which alkylenedicarboxonium ions (diprotonated dicarboxylic acids) can be dehydrated diminishes with decreasing separation between the acid functions. Pimelic, adipic, and glutaric acids cleave under conditions similar to the protonated monocarboxylic acids previously studied[4] ($t_{1/2}$ about 1 hr at $-20°$), the changes in the nmr spectra being consistent with the formation of a monooxocarbonium–monocarboxonium ion having the structure III.

III
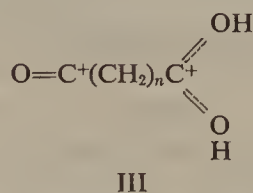
The downfield shifts of the methylene protons on cleavage of the diprotonated dicarboxylic acid to the monooxocarbonium ion are very similar to the shifts found in the dehydration of protonated alkylcarboxylic acids and are about 1.0, 0.5, and 0.2 ppm for the

methylene protons α, β, and γ to the oxocarbonium center in both series.

Succinic acid cleaves to the extent of *ca.* 50% in FSO_3H–SbF_5–SO_2, indicating that an equilibrium is reached between the diprotonated acid and the monooxocarbonium ion, as is observed with protonated monocarboxylic acids in H_2SO_4–oleum[10] or in HF–BF_3.[11] Increasing the strength of the acid by using neat FSO_3H–SbF_5 permitted the reaction to go to completion.

Malonic (and probably oxalic) acid did not give an oxocarbonium ion under experimental conditions, thus setting a limit on the strength of the acid system.

Chemical shifts and coupling constants of the alkylenemonooxocarbonium–monocarboxonium ions are tabulated in Table II and spectra of the ions are shown in Figures 5 and 6.

Table II. Nmr Chemical Shifts and Coupling Constants of Alkylenemonooxocarbonium–Monocarboxonium Ions

$$[O\overset{+}{=}CC\overset{\alpha}{H_2}C\overset{\beta}{H_2}(C\overset{\gamma}{H_2})_nCO_2H_2^+]$$

Acid precursor	Temp, °C	OH	CH₂ (α)	CH₂ (β)	CH₂ (γ)
$(CH_2)_2(COOH)_2$	-90	-14.43 -14.27	-5.15^a	-4.47	...
$(CH_2)_3(COOH)_2$	-70	-13.47 -13.37	-4.70^b	-3.80^b	-3.2^c
$(CH_2)_4(COOH)_2$	-60	-13.15 -12.92	-4.60^b	-3.62^b	-2.8^d
$(CH_2)_5(COOH)_2$	-60	-12.85 -12.58	-4.48^b	-3.47^b	-2.8^d

^{a} Broad triplet. ^{b} Triplet, $J = 7$ Hz. ^{c} Pentuplet, $J = 7$ Hz. ^{d} Multiplet.

Formation of Alkylenedioxocarbonium Ions. Loss of a second water molecule from protonated glutaric, adipic, and pimelic acids occurs between -20 and 10°. In the cases of adipic and pimelic acids, the acid functions are sufficiently well separated for the loss of the second water molecule to occur at a similar rate to that of the first, giving generally a mixture of the mono- and dioxocarbonium ions. Assignments for these species given in Table II are based on observations of the changes of the spectra with time. Glutaric acid could only be taken to a 50% equilibrium mixture of the dioxo- and monooxocarbonium ions in neat FSO_3H–SbF_5 at 0°. Increasing the temperature to $+50°$ caused no significant change in the equilibrium position.

Table III. Nmr Chemical Shifts (in ppm) and Coupling Constants (in Hz) of Alkylenedioxocarbonium Ions in FSO_3H–SbF_5 at 0°

Dioxocarbonium ion	CH₂ (α)	CH₂ (β)	CH₂ (γ)
$\overset{+}{O}C(CH_2)_3\overset{+}{C}O$	-4.90^a	-4.17^b	...
$\overset{+}{O}C(CH_2)_4\overset{+}{C}O$	-4.72^b	-3.02^b	...
$\overset{+}{O}C(CH_2)_5\overset{+}{C}O$	-4.55^a	-2.82^b	-2.20^b

^{a} Triplet, $J = 7$ Hz. ^{b} Multiplet.

(10) N. C. Deno, C. U. Pittman, Jr., and M. J. Wisotsky, *J. Am. Chem. Soc.*, 86, 4370 (1964).
(11) H. Hogeveen, *Rec. Trav. Chim.*, 86, 289 (1967).

$$O=\overset{+}{C}-CH_2CH_2-\overset{+}{C}O_2H_2$$
$$\qquad \alpha \qquad \beta$$

Figure 5.

$$O=\overset{+}{C}-CH_2CH_2CH_2\overset{+}{C}O_2H_2$$
$$\qquad \alpha \quad \beta \quad \gamma$$

Figure 6.

$$O=\overset{+}{C}-CH_2CH_2CH_2\overset{+}{C}O_2H_2$$
$$\qquad \alpha' \qquad \text{and}$$
$$O=\overset{+}{C}-CH_2CH_2CH_2\overset{+}{C}=O$$
$$\qquad \alpha$$
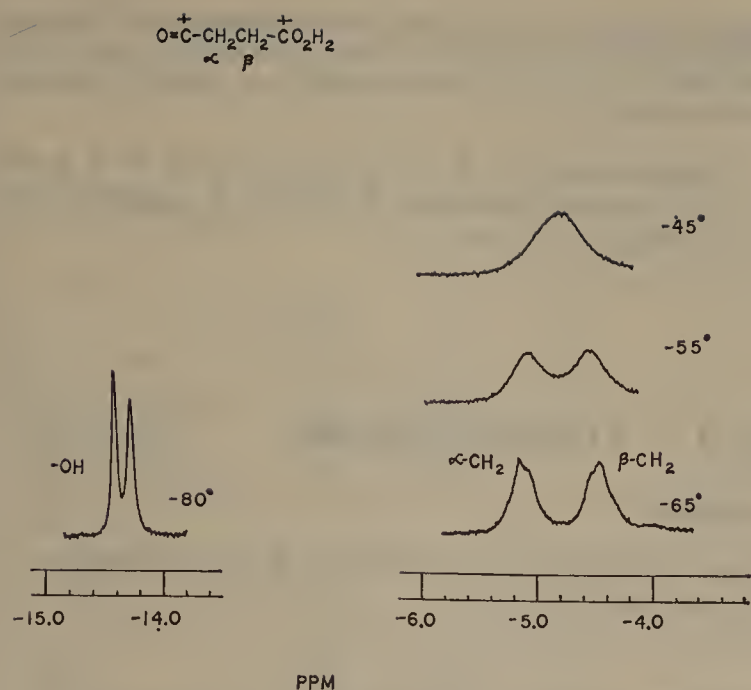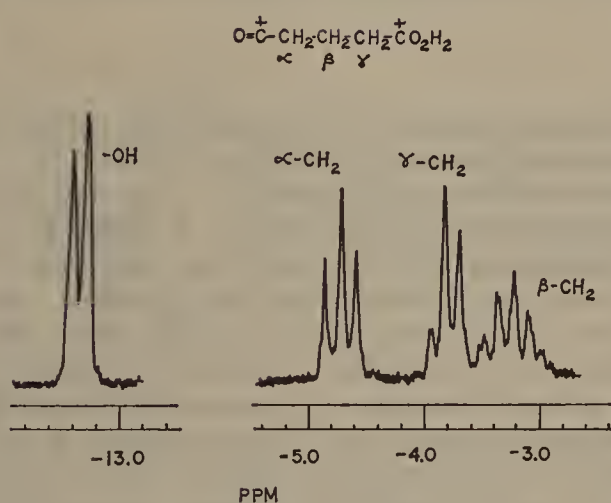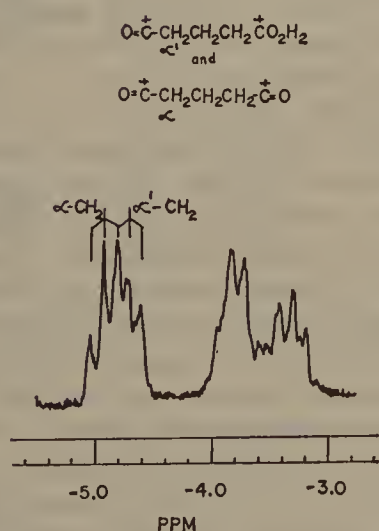
Figure 7.

The nmr spectra of the dioxocarbonium ions (see Table III and Figures 7–9) agree well with those previously reported for solutions of the SbF$_6^-$ salts in SO$_2$ solution[4] though, as in the case of the formation of oxocarbonium ions from the protonated monocarboxylic acids, a downfield medium effect was noted. The fact that succinic acid would not give a dioxocarbonium ion is consistent with the observation that the

$$O=\overset{+}{C}-(CH_2)_4-\overset{+}{C}=O$$

Figure 8.

$$O=\overset{+}{C}-(CH_2)_5\overset{+}{C}=O$$
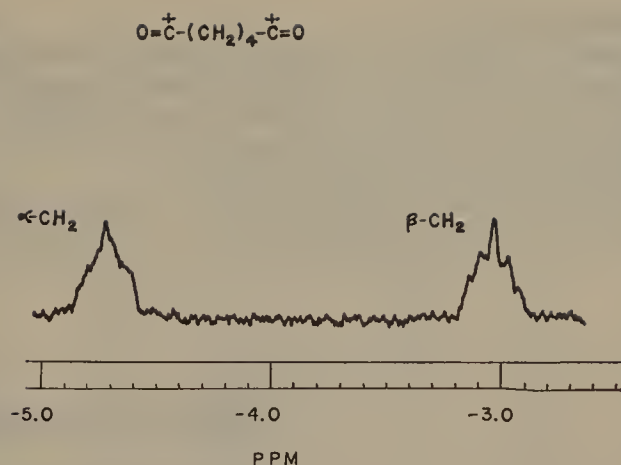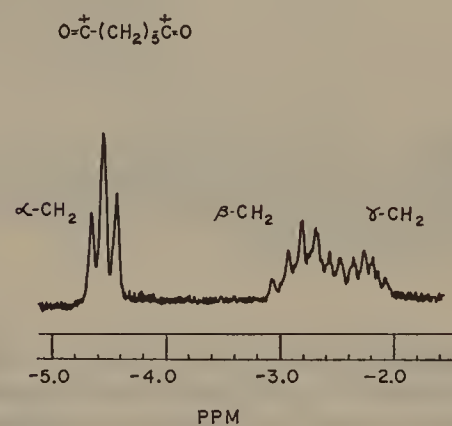
Figure 9.

diacid fluoride gives only a monooxocarbonium ion mono-donor–acceptor complex with SbF$_5$.[4]

Protonated Anhydrides and Their Cleavage. The anhydrides of succinic and glutaric acids were examined in FSO$_3$H–SbF$_5$–SO$_2$ solutions as an alternative route to the oxocarbonium ions. The protonated anhydrides could not be observed even when solutions were prepared and examined at −80°. In both cases the nmr spectra obtained corresponded to the alkylenemonooxocarbonium–monocarboxonium ion formed from the protonated dicarboxylic acids. The existence of protonated anhydrides as intermediates was suggested by the observation that the two triplets in the monooxocarbonium ion from succinic acid collapsed reversibly to a single peak at −45°, suggesting an intramolecular rearrangement through a cyclic intermediate.

$$H_2\overset{+}{O}_2C \ (CH_2)_2 \ \overset{+}{C}O_2 \ \rightleftharpoons \ \underset{HO^+ \quad O \quad {}^+OH}{\overset{CH_2-CH_2}{\diagup \ \diagdown}} \ \rightleftharpoons \ O\overset{+}{C} \ (CH_2)_2CO_2H_2^+$$
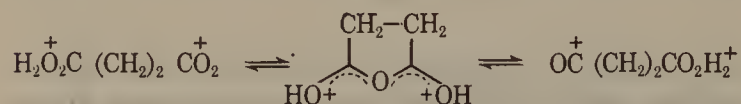
The observation that diprotonated cyclic anhydrides exist in the open-chain form led us to examine other anhydrides. Acetic and propionic anhydrides also show similar behavior and exist in FSO$_3$H–SbF$_5$–SO$_2$ as a 1:1 mixture of the oxocarbonium ion and the protonated acid.

$$(RCO)_2O \xrightarrow[-80°]{FSO_3H-SbF_6-SO_2} R\overset{+}{C}O + RCO_2H_2^+$$
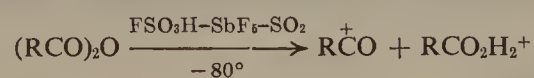
This observation is in accord with the reported fourfold depression of freezing point by acetic anhydride in sulfuric acid.[12] Succinic anhydride was reported to be only partially protonated in sulfuric acid.[12]

(12) R. J. Gillespie and J. A. Leisten, *Quart. Rev.* (London), **8**, 40 (1954).

Experimental Section

Materials. All dicarboxylic acids and anhydrides were reagent grade commercial chemicals. They were used without further purification except for glutaric anhydride which was found to be contaminated with the acid. Repeated recrystallizations from diethyl ether were used to purify this compound.

Formation of Ions and Their Nmr Spectra. A Varian A-56-60A nmr spectrometer with variable-temperature probe was used for all spectra. Solutions were prepared at $-80°$ using a $1:1$ M solution of HSO_3F–SbF_5 and SO_2 as a diluent according to procedures described previously.[4] Chemical shifts were referred to external capillary TMS.

Stable Carbonium Ions. L.[1] Protonated Imines

George A. Olah and Paul Kreienbühl[2]

Contribution from the Department of Chemistry, Case Western Reserve University, Cleveland, Ohio 44106. Received April 21, 1967

Abstract: Nuclear magnetic resonance study of protonated aldimines and ketimines in fluorosulfonic acid, fluorosulfonic acid–antimony pentafluoride, and deuteriosulfuric acid–antimony pentafluoride solution indicates the predominance of immonium structure ($R_1R_2C{=}N^+HR_3$), with only limited contribution of aminocarbonium ion forms ($R_1R_2C^+{-}NHR_3$).

The properties of the imine bond ($>C{=}N$) and the carbonyl bond ($>C{=}O$) are related and in some of their reactivity, imines and carbonyl compounds show similarity.[3]

In continuation of our previous work on protonated aldehydes,[4] ketones,[5] and esters,[6] we have now extended our investigation to protonated imines. We were particularly interested whether the contribution of aminocarbonium ion forms, as suggested by Deno,[7] could be substantiated.

Results and Discussion

Protonated aldimines and ketimines were observed by nmr spectroscopy in the extremely strong acid systems, FSO_3H, FSO_3H–SbF_5, or D_2SO_4–SbF_5 using SO_2 as diluent.
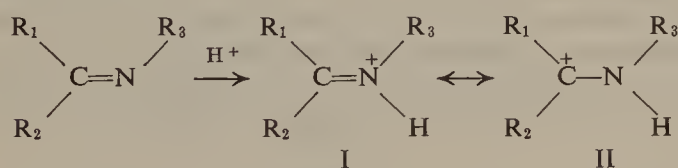
The protonated imines give well-resolved nmr spectra. However, the N–H proton appears to broaden due to the quadrupole interaction of the nitrogen-14 and cannot always be observed. The failure to observe the N–H proton in some cases is not due to rapid exchange since splitting of adjacent protons by the N–H proton is always observed. Coupling contributes to N–H peak broadenings. Nuclear magnetic resonance spectroscopy offers a possibility of investigating whether the

immonium salt structure I is the only contributing form of protonated imines or if there is evidence for some aminocarbonium ion character (II). The nmr data of protonated imines are summarized in Table I. Neat N-propylidenemethylamine shows a long-range coupling from the C-methyl to the N-methyl groups, $J_{H-H}trans = 1.35$ Hz, $J_{H-H}cis = 0.7$ Hz, which is analogous to homoallylic coupling. The most commonly observed examples of homoallylic coupling are interactions between vicinal vinylic protons in various butene derivatives,[8] and the size of such a coupling constant was proposed as a possible measure of the π character of a $C{=}C$ double bond.[9] The nmr spectrum of the protonated N-propylidenemethylamine in SO_2 at $-20°$ (Figure 1) shows a doublet for the N-methyl groups ($J_{HNCH_3} = 5.0$ Hz) at -3.96 ppm. The C-methyl group appears as two lines, at -3.08 and -3.02 ppm. There is no long-range coupling observable. The chemical shift of a methyl group adjacent to a positive carbon atom is expected at -4.5 ppm.[10] This is at substantially lower field than is observed in protonated N-propylidenemethylamine. However, the result could be understood in two ways: either as an immonium salt (I) where the two C-methyl groups are nonequivalent, or as an aminocarbonium ion (II), where the C-methyl groups are coupled to the NH proton through the positively charged C atom and split into a doublet. To distinguish between the two possibilities, we obtained the nmr spectrum in D_2SO_4–SbF_5 in SO_2. The two C-methyl groups remain unchanged. Therefore they are nonequivalent, clearly indicating that there is no free rotation around the carbon–nitrogen bond. Thus the aminocarbonium ion form can be eliminated.[4]

The nmr spectra indicate that protonated N-propylidenemethylamine exists mainly as immonium salt

(1) Part XLIX: G. A. Olah and A. M. White, *J. Am. Chem. Soc.*, **89**, 4752 (1967).

(2) National Science Foundation Postdoctoral Research Investigator, 1966–1967.

(3) For reviews, see M. M. Spring, *Chem. Rev.*, **26**, 297 (1940).

(4) G. A. Olah, D. H. O'Brien, and M. Calin, *J. Am. Chem. Soc.*, **89**, 3582 (1967).

(5) G. A. Olah, M. Calin, and D. H. O'Brien, *ibid.*, **89**, 3586 (1967).

(6) G. A. Olah, D. H. O'Brien, and A. M. White, *ibid.*, in press.

(7) N. C. Deno, *Progr. Phys. Org. Chem.*, **2**, 129 (1963).

(8) S. Sternhall, *Rev. Pure Appl. Chem.*, **14**, 15 (1964).

(9) G. O. Dudek, *J. Am. Chem. Soc.*, **85**, 694 (1963).

(10) G. A. Olah, E. B. Baker, J. C. Evans, W. S. Tolgyesi, J. S. McIntyre, and I. Bastien, *ibid.*, **86**, 1360 (1964).

Table I. Nmr Chemical Shifts and Coupling Constants of Protonated Imines[a]

	Temp, °C	R₁ = CH₃ −δ, ppm	R₁ = CH₃ J, Hz	R₁ = CH₃ Δδ, ppm	R₂ = CH₃ −δ, ppm	R₂ = CH₃ Δδ, ppm	R₃ = CH₃ −δ, ppm	R₃ = CH₃ J, Hz	R₃ = CH₃ Δδ, ppm	NH −δ, ppm
Neat	−30	1.88 (4)	1.35	...	1.75 (4)	...	2.95 (cm)	...	...	...
HSO₃F–SbF₅–SO₂	−60	2.82 (1)	0	0.94	2.73 (1)	0.98	3.66 (2)	5.1	0.71	9.53
HSO₃F–SbF₅	−20	3.08 (1)	0	1.20	3.02 (1)	1.27	3.96 (2)	5	1.01	9.83
D₂SO₄–SbF₅–SO₂	−30	2.88 (1)	0	1.00	2.81 (1)	1.05	3.68 (1)	≈0	0.73	...
		R₁ = H			R₂ = phenyl[b]		R₃ = CH₃			
Neat	38	8.04 (4)	1.6	...	7.54 (cm)	...	3.33 (2)	1.6	...	...
CDCl₃	−30	7.99 (4)	1.8	...	7.45 (cm)	...	3.36 (2)	1.8	...	...
HSO₃F	−30	8.81 (2)	17.3	−0.77	8.03 (cm)	−0.49	3.84 (2)	4.5	−0.51	10.0
HSO₃F–SbF₅–SO₂	−30	8.70 (2)	16.9	−0.72	7.83 (cm)	−0.38	3.72 (2)	4.0	−0.36	N.o.
D₂SO₄–SbF₅–SO₂	−20	8.91 (b)	≈0	−0.87	8.16 (cm)	−0.62	4.03 (b)	≈0	−0.70	...
		R₁ = H			R₂ = R₃ = phenyl[b,c]					
SO₂	−20	8.17 (1)	...	...	7.27 (cm)	...				...
HSO₃F–SO₂	−20	9.15 (2)	18	−0.98	7.85 (cm)	−0.58				N.o.[d]
HSO₃F–SbF₅–SO₂	−40	9.35 (2)	18	−1.18	8.22 (cm)	−0.95				N.o.
D₂SO₄–SbF₅–SO₂	−20	9.08 (6)	...	−0.91	7.83 (cm)	−0.56				...
		R₁ = H			R₂ = phenyl[b]		R₃ = Cl–phenyl			
SO₂	−30	8.32 (1)	...	...	7.58 (cm)	...	7.13		...	...
HSO₃F–SO₂	−30	9.33 (2)	17.4	−1.01	7.90 (1)	−0.32	8.25		−1.12	N.o.
HSO₃F–SbF₅–SO₂	−30	9.27 (2)	17.2	−0.95	7.85 (1)	−0.27	8.18		−1.05	N.o.
D₂SO₄–SbF₅–SO₂	30	9.45 (1)	... (b)	−1.13	8.05 (1)	−0.47	8.40		−1.27	N.o.
		R₁ = CH₃			R₂ = phenyl[b]		R₃ = CH₃			
Neat	38	1.87 (4)	0.8	...	7.55 (cm)	...	3.16 (4)	0.8	...	...
HSO₃F–SO₂	−40	2.97 (1)	...	−1.10	7.92 (cm)	−0.37	3.70 (2)	5.1	−0.54	10.0
HSO₃F–SbF₅–SO₂	−40	3.00 (1)	...	−1.13	7.95 (cm)	−0.40	3.72 (2)	5.5	−0.56	N.o.
D₂SO₄–SbF₅–SO₂	−30	3.18 (1)	...	−1.31	8.18 (cm)	−0.63	3.92 (1)	... (6)	−0.76	N.o.
		R₁ = R₂ = phenyl[b,c]					R₃ = CH₃			
CDCl₃	−20	7.32 (cm)	0.9	...			3.24 (1)	...	...	...
HSO₃F–SbF₅–SO₂	−30	8.00 (cm)	0.87	−0.68			3.79 (2)	5.5	−0.55	9.7
D₂SO₄–SbF₅–SO₂	−30	7.75 (cm)	0.68	−0.43			3.85 (1)	...	−0.61	...

[a] −δ = shift in parts per million from external capillary of TMS. Figures in parentheses represent multiplicity of peaks, cm = complex multiplex, b = broad single line. [b] For phenyl, we measured the shift of the middle of the complex multiplex. [c] The two phenyl patterns appear (especially in the starting material) in the same region and cannot be clearly distinguished. [d] Not observable due to quadruple broadening and coupling.

(I) with only minor contribution of the aminocarbonium form (II).

In aryl-conjugated systems it is expected that the aminocarbonium ion form should be stabilized. We prepared N-benzylidenemethylamine as a mixture of the two geometric isomers (see Experimental Section).

The nmr spectrum in SO₂ shows two quadruplets for the methine proton at −8.38 ppm for the *anti* form IV and at 8.15 for the *syn* isomer V, and the two methyl doublets at −3.47 (IV) and −3.27 (V) ppm. The coupling constants J_{HCNCH_3} are 1.9 Hz (for IV) and 1.6 Hz (V). There was controversy over whether such isomers
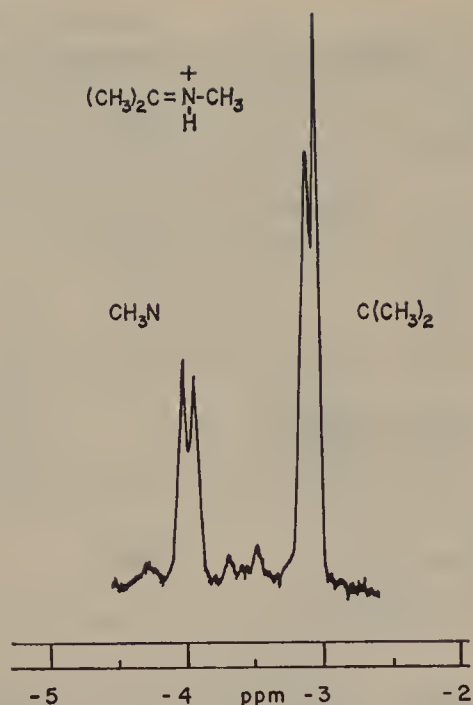
Figure 1.
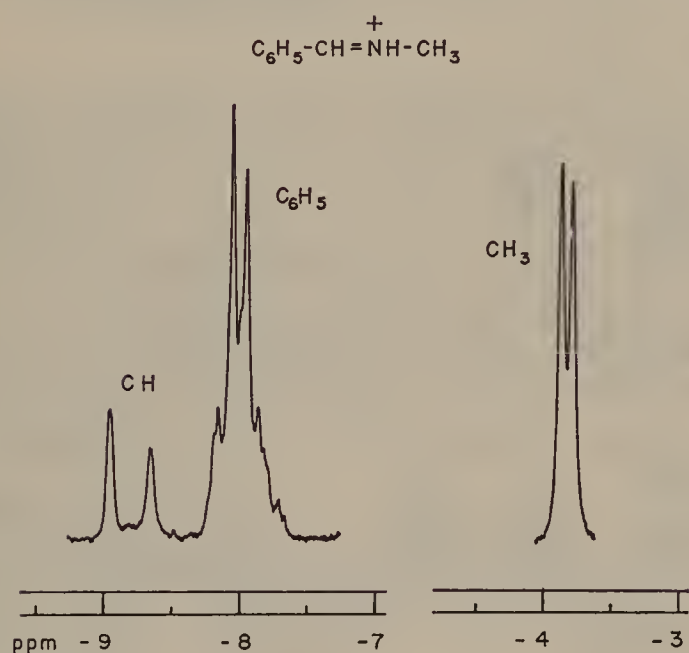
Figure 2.

could be observed until *cis-p*-chlorobenzophenone methylimine was obtained as a crystalline solid and found to rearrange to the *cis–trans* equilibrium mixture.[11,12] *anti*-Benzylidenemethylamine (neat) shows the methine proton as a quadruplet at -8.04 ppm ($J_{H-H} = 1.6$ Hz), the phenyl protons (main peak) at -7.54 ppm, and the methyl protons (doublet) at -3.33 ppm ($J_{H-H} = 1.6$ Hz).[13]
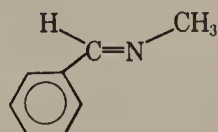
IV
anti
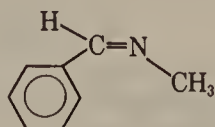
V
syn

In the protonated imine (Figure 2) the methine proton is shifted to -8.8 ppm (broad doublet, $J_{H-H} = 17$

(11) R. Kuhn and H. Schretzman, *Ber.*, **90**, 560 (1957).
(12) D. Y. Curtin and J. W. Hausser, *J. Am. Chem. Soc.*, **83**, 3474 (1961).
(13) R. W. Fessenden and J. S. Waugh, *J. Chem. Phys.*, **30**, 948 (1959).
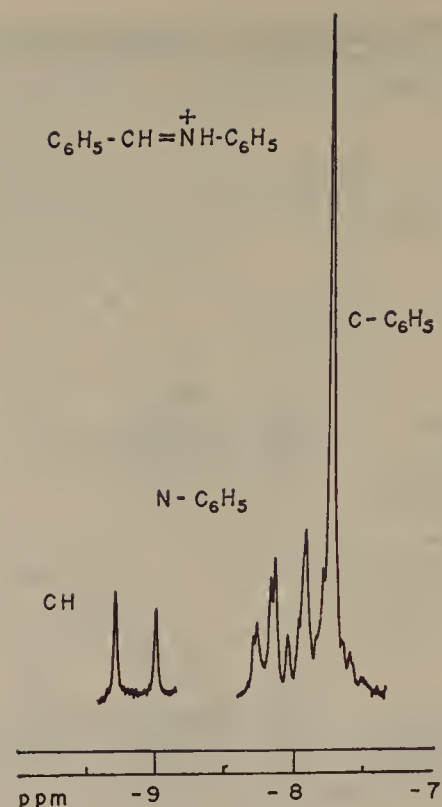
Figure 3.

Hz), the phenyl protons to -8.03 ppm, and the methyl protons to -3.84 ppm ($J_{H-H} = 4.5$ Hz). These data indicate the *trans*-immonium form VI, based on the 17-Hz coupling.
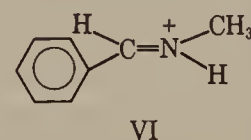
VI

The size of the *trans* coupling constants through a double bond does not change much in isoelectronic molecules (see Table II). This close agreement shows that in proton spin–spin coupling, changes of geometry and bond character have much more effect upon the coupling constants than charge effects and the kind of atom bearing the hydrogen. The chemical shift and coupling data indicate that the immonium form is predominant over the aminocarbonium ion form, despite the fact that the latter should be stabilized by delocalization by the neighboring phenyl group. Similar conclusions were obtained from the investigation of protonated N-benzylideneaniline (VII) (Figure 3), N-benzylidene-*p*-chloroaniline (VIII) (Figure 4), N-α-methylbenzylidenemethylamine (IX) (Figure 5), and benzhydrylidenemethylamine (X) (Figure 6). In all these cases, the aminocarbonium ion form should be
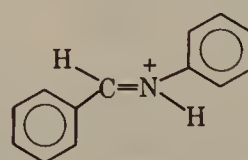
VII

VIII

IX

X
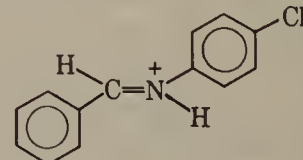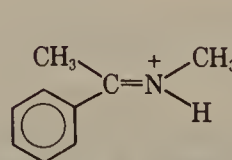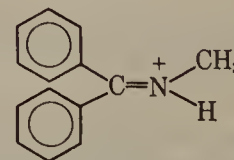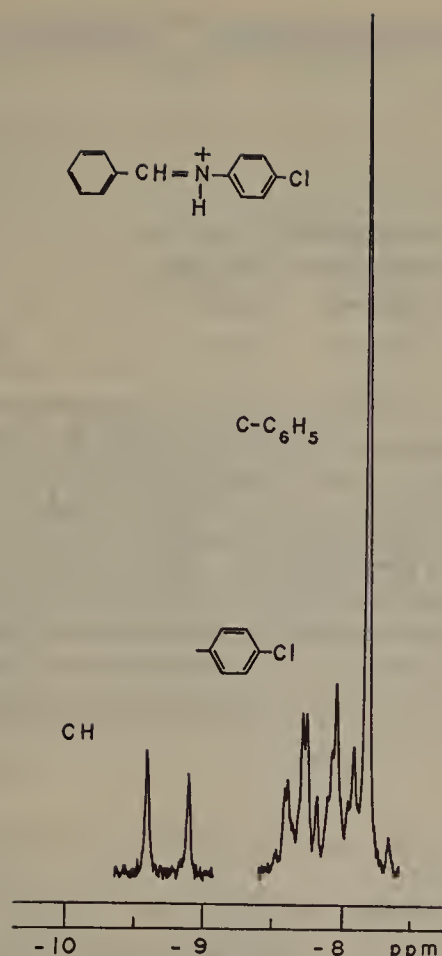
Figure 4.

Figure 5.

stabilized by neighboring phenyl group(s). However, the nmr data still indicate the predominance of the immonium ion form.

Table II. *trans* Coupling Constants in Isoelectronic Molecules

	trans $J_{HC=CH}$, Hz	Lit.
$\begin{smallmatrix}C_6H_5\\H\end{smallmatrix}>C=C<\begin{smallmatrix}H\\CH_3\end{smallmatrix}$	15.6	
$\begin{smallmatrix}CH_3\\H\end{smallmatrix}>C=O^+-H$	19.5	4
$\begin{smallmatrix}C_6H_5\\H\end{smallmatrix}>C=N^+<\begin{smallmatrix}H\\CH_3\end{smallmatrix}$	17.4	

Figure 6.

Experimental Section

N-Benzylidenemethylamine, N-benzylideneaniline, and N-benzylidene-*p*-chloroaniline were reagent grade and were used without further purification.

N-Isopropylidenemethylamine. Acetone and methylamine (ratio 1:1.5) were condensed in a pressure tube. Solid KOH was added to bind the water which is formed during the reaction. The mixture was heated to 120° overnight. After distillation, N-isopropylidenemethylamine was obtained in about 45% yield, bp 65°.

N-Benzylidenemethylamine. To a large excess of liquid methylamine at −40° benzaldehyde was added dropwise, and the mixture was allowed to warm slowly to room temperature. The product was purified by vacuum distillation from KOH. The obtained material was found (nmr) to be a mixture of *syn-* and *anti-*N-benzylidenemethylamine.

α-Methylbenzylidenemethylamine. A mixture of 60 g of acetophenone, 31 g of methylamine, and 56 g of potassium hydroxide was heated for 6 hr at 140°. The crude product was vacuum distilled. Separation of the imine and acetophenone was accomplished by preparative gas chromatography (Airograph Autoprep, 20-ft silicon column at 180°).
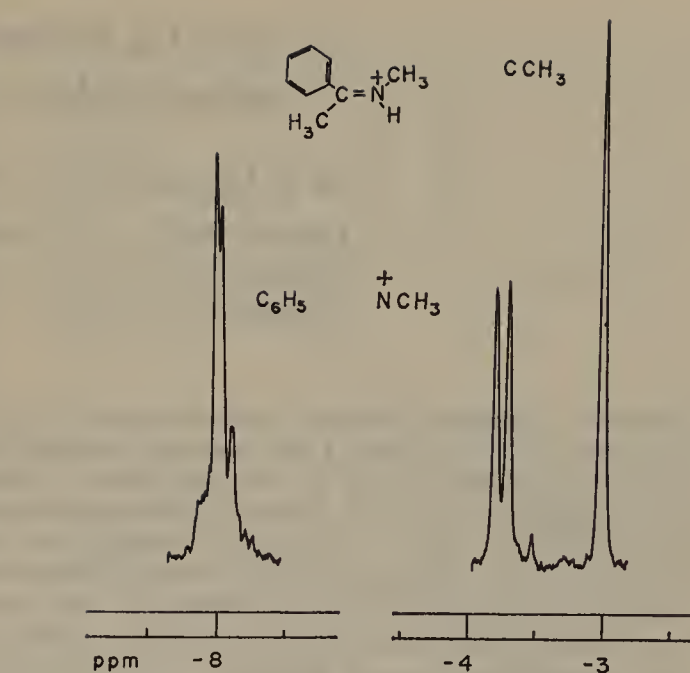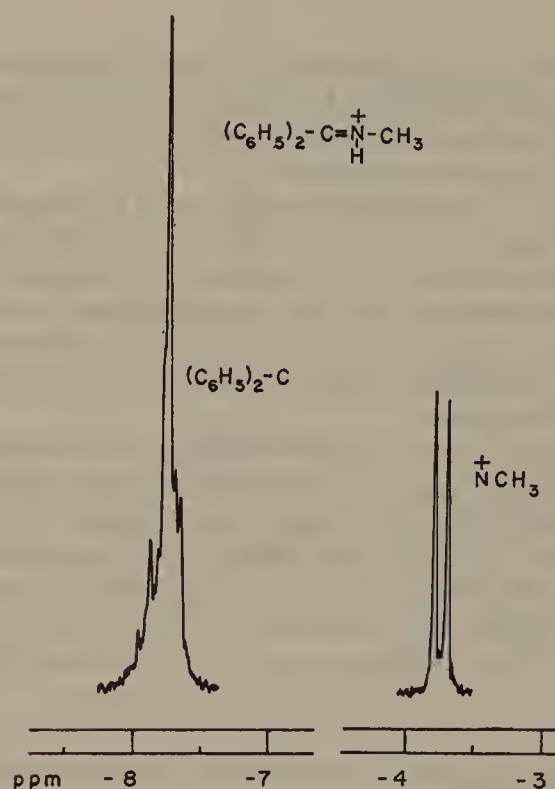
Benzhydrilidenemethylamine was prepared from benzophenone and methylamine according to the method of Hauser, *et al.*[14]

Protonation of Imines. The protonated imines were observed by adding the corresponding imine in SO₂ to the stirred acid solution (FSO₃H, FSO₃H–SbF₅, D₂SO₄–SbF₅) diluted with SO₂ at temperatures indicated in Table I.

Nmr Spectra. A Varian Associates Model A-56-60-A nmr spectrometer with a variable-temperature probe was used for all nmr spectra. External capillary of TMS was used as reference.

(14) C. R. Hauser, R. M. Manyik, W. R. Brasen, and P. L. Bayless, *J. Org. Chem.*, **20**, 1119 (1955).

1-Cyano-1,2,3-triazole–α-Diazo-N-cyanoimine Tautomers from Cyanogen Azide and Acetylenes

M. E. Hermes and F. D. Marsh

Contribution No. 1276 from the Central Research Department, Experimental Station, E. I. du Pont de Nemours and Company, Wilmington, Delaware 19898. Received February 11, 1967

Abstract: Cyanogen azide reacts with acetylene to form a 1:1 adduct, in 77% yield, which is a ring–chain tautomeric mixture of 1-cyano-1,2,3-triazole and α-diazo-N-cyanoethylidenimine. It has been shown by infrared, ultraviolet, and nmr spectra that the equilibrium is temperature and solvent sensitive and both tautomers have been identified in solution by decomposition with hydrochloric acid to 1,2,3-triazole hydrochloride and nitrogen and chloroacetaldehyde, respectively. Methyl- and dimethylacetylenes give similar tautomeric mixtures with cyanogen azide. The cyanogen azide–ethoxyacetylene adduct is formed in 87% yield and exists exclusively as the open-chain ethyl α-diazo-N-cyanoacetimidate. This diazo compound gives ethyl chloroacetate and nitrogen on treatment with HCl and acts as a 1,3-dipole on addition to norbornene and dimethyl acetylenedicarboxylate to give pyrazoline and pyrazole derivatives. Thermochromic and spectral behavior of 1-cyanobenzotriazole, formed from benzotriazole anion and cyanogen chloride in 67% yield, indicates that some ring opening to a diazo-N-cyanoimine may be occurring.

This paper discusses the reaction of acetylenes with cyanogen azide (N_3CN) without loss of nitrogen to form 1-cyano-1,2,3-triazoles which are in equilibrium with α-diazo-N-cyanoimines.

We have reported the preparation of cyanogen azide, its reactions with olefins,[1] and its pyrolysis to form azodicarbonitrile.[2] The reaction of cyanogen azide with cyclooctatetraene[3] and norbornadiene[4] have been described, and the decomposition of the azide to form cyanonitrene which reacts with alkanes[5] and aromatics[6] has been reported.

In general, cyanogen azide reactions carried out above 50° proceed by unimolecular decomposition with loss of nitrogen to an excited singlet cyanonitrene which may or may not form the more stable triplet depending upon reaction conditions,[7,8] followed by attack on the substrate. Below 50°, the azide is usually the reacting species. The acetylene reaction is of this latter type.

Results

Cyanogen azide reacts with acetylene at 45° to give 77% of a 1:1 adduct that is colorless below its melting point (33°) but is yellow in the melt or in solution. The substance (1) is a tautomeric composition of 1-cyano-1,2,3-triazole (1a) and α-diazo-N-cyanoethylidenimine (1b). Evidence for this ring-chain equilibrium is

based on infrared and nmr spectral data and chemical transformations.

Spectral Evidence for 1a ⇌ 1b. The infrared spectrum of **1** (Table I) is markedly temperature dependent. The spectrum at −10° in KBr has —C≡N absorption at 4.43 μ and only very weak absorption from 4.5 to 7 μ. In contrast, the spectrum at 35° has additional strong

Table I. Properties of **1**

Mp, +33°
Infrared (35°, liquid melt): 3.19, 4.43, 4.60, 4.71, 6.40, 7.07, 7.20, 7.65, 7.95, 10.28, 11.10, 12.75 μ
Infrared (35°, KBr wafer): 3.19, 4.43, 4.62, 4.70, 6.40, 7.07, 7.20, 7.63, 7.96, 10.26, 11.10, 12.75 μ
Infrared (−10°, KBr wafer): 3.19, 4.43, 7.04, 7.62, 7.98, 9.54, 10.24, 11.00, 12.45 μ
Ultraviolet: $\lambda_{max}^{CH_2Cl_2}$ ... 309.5 mμ (ε 1990)
$\lambda_{max}^{CH_3CN}$ 229 mμ (ε 4800); 307 mμ (ε 2280)
$\lambda_{max}^{H_2O}$ 232 mμ (ε 2980); 309 mμ (ε 7120)
Nmr (pure liquid, 35°): τ 1.82 (1 H, doublet, J = 1.7 cps), τ 2.73 (1 H, broad singlet)
Solution, CDCl₃: see Figure 1, Table II.

absorption at 4.62, 4.70, and 6.40 μ, indicating diazo and >C=N—CN groups are present.[9] The liquid spectrum at 35° resembles the KBr spectrum, and comparison of absorption in the 9–13-μ region of the liquid sample with that region in the spectrum at −10° shows that there is some 1-cyanotriazole present in the liquid state.

The ultraviolet spectrum of **1** in water, acetonitrile, and dichloromethane (Table I) shows little change in wavelength with solvent variation and the solutions obey Beer's law. However, the extinction coefficient is quite solvent dependent. The shorter wavelength band is less intense in water than in acetonitrile while the long wavelength band becomes more intense from dichlorometh-

(1) F. D. Marsh and M. E. Hermes, *J. Am. Chem. Soc.*, **86**, 4506 (1964).

(2) F. D. Marsh and M. E. Hermes, *ibid.*, **87**, 1948 (1965).

(3) A. G. Anastassiou, *ibid.*, **87**, 5512 (1965).

(4) A. G. Anastassiou, *J. Org. Chem.*, **31**, 1131 (1966).

(5) A. G. Anastassiou, F. D. Marsh, and H. E. Simmons, *J. Am. Chem. Soc.*, **87**, 2296 (1965).

(6) F. D. Marsh and H. E. Simmons, *ibid.*, **87**, 3529 (1965).

(7) G. J. Pontrelli and A. G. Anastassiou, *J. Chem. Phys.*, **42**, 3755 (1965).

(8) A. G. Anastassiou, *J. Am. Chem. Soc.*, **89**, 3184 (1967).

(9) The 4.43-μ band at the higher temperature does not decrease in intensity, which indicates that this band arises from nitrile in both compounds. Thus, it appears that diazo absorbs as a doublet at 4.62 and 4.70 μ. The 6.4-μ band at 35°, the strongest band in the spectrum, is also characteristic of the C=N bond in alkylidene cyanamides prepared from olefins and N_3CN.

ane to acetonitrile to water presumably as the open-chain form predominates in solution in the more polar solvents.[10]

Complex changes in the nmr spectra occur with temperature (Figure 1, Table II). The neat liquid spectrum consists of two areas of absorption each representing one proton. At τ 1.82 a sharp doublet ($J = 1.7$ cps) and at τ 2.73 a broad single peak are observed. At $-60°$ in $CDCl_3$ two sharp doublets are observed of equal weight with $J = \sim1.5$ cps at τ 1.60 and 2.02. On warming, the lower field peak becomes somewhat broader, with increasing temperature, but remains a doublet with slightly greater separation (~2.2 cps). The position of this resonance remains essentially constant throughout. The higher field resonance undergoes remarkable changes. On warming of the solution from -60 to $+80°$, this peak moves upfield with successive broadening, sharpening, and broadening.

Table II. Chemical Shift of Proton Resonance of **1** in $CDCl_3$

Temp, °C	Low field, τ	High field, τ
-60^a	1.60	2.02
-40	1.47	2.06
-10	1.47	2.08
20	1.44	2.19
50	1.38	2.21
80	1.38	2.36

^{a} 5% in $CDCl_3$. All others are 20% in $CDCl_3$.

A possible interpretation of these results involves not only the ring-chain tautomerism **1a** $\rightleftharpoons$ **1b** but also the syn–anti relationship of the —HC≡N—CN group and the cis–trans orientation of the diazo and N-cyanoimine group of **1b**.

Since the absorption intensities remain 1:1 throughout the temperature range, it is probably correct to assign each absorption to a specific proton. Thus the low-field absorption is believed to be the C_5–H of the triazole and, coincidently, the —HC≡NCN of the open-chain form. The chemical shift of the C_4– and C_5–H's of 12 1-substituted 1,2,3-triaz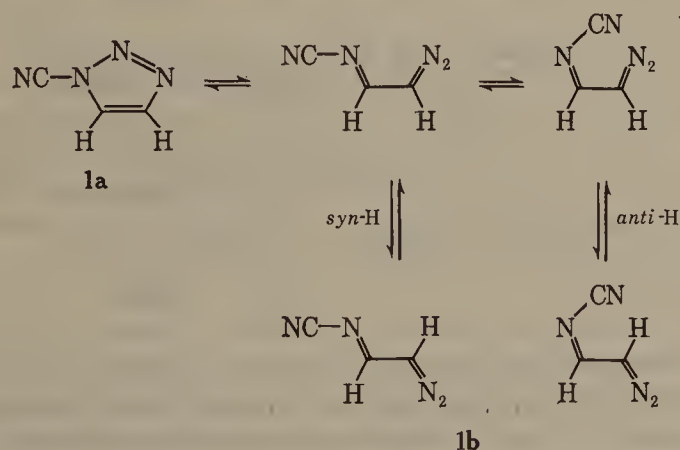oles has been found to vary between τ 1.8 and 2.8[11] with $J \cong 1$ cps. Thus one may presume that the $-60°$ spectrum fairly represents **1a**.

As the temperature rises, the rate of **1a** $\rightleftharpoons$ **1b** increases and, as has been shown by infrared, the propor-

(10) The ultraviolet spectrum of **1** does not resemble that of α-diazobutyraldehyde, prepared by J. Kučera and Z. Arnold, *Tetrahedron Letters*, 1109 (1966); λ_{max} 249 mμ (ϵ 10,000), 284 mμ (ϵ 6450), and 383 mμ (ϵ 32).

(11) R. A. Clement, personal communication.
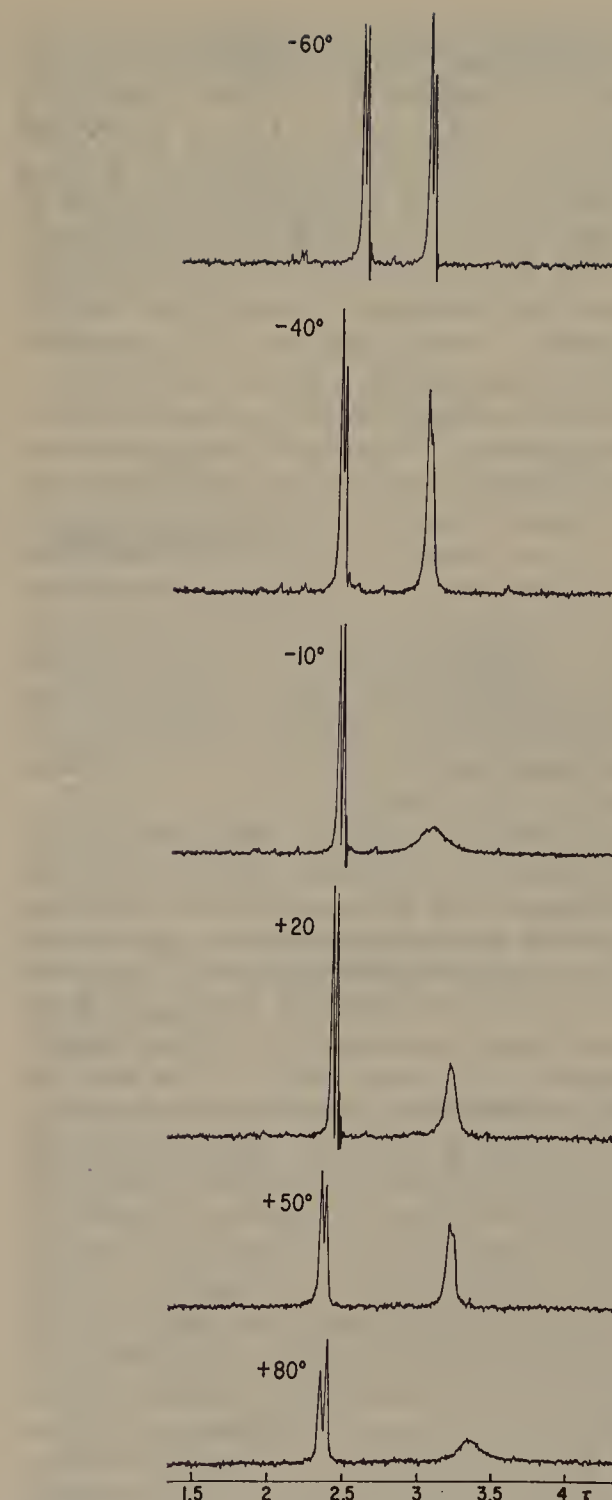
Figure 1. Nmr spectra of the cyanogen azide–acetylene adduct at 60 Mc.

tion of **1b** is also higher. At $-10°$ in solution, we observe broadening and upfield displacement of the higher field peak as averaging of the C_4–H of **1a** and the methine CH of **1b** occurs. A large shift might be expected since Kaplan and Meloy[12] found the methine CH absorption of the cis form of diazoacetaldehyde at τ 4.3. It is clear that this resonance of pure **1b** does not approach that value. The broad resonance at this point indicates the rate of **1a** $\rightleftharpoons$ **1b** is still slow compared to the chemical shift between the high-field protons of the two forms. Further increase in temperature to $+20°$ sharpens the high-field resonance and moves it to still higher field, indicating that the **1a** $\rightleftharpoons$ **1b** rate is fast enough so that the time-averaged resonance line of **1a** and **1b** is approached.

(12) F. Kaplan and G. K. Meloy, *J. Am. Chem. Soc.*, **88**, 950 (1966), discuss the cis–trans relationships of α-diazoacetaldehyde and α-diazo ketones.

At this point, let us consider evidence bearing on the possible configurations of **1b**. Isomerization of the cyano group of N-cyanoimines has been observed in isopropylidene cyanamide, prepared from N_3CN and propylene.[13] At 35° the compound has two sharp resonance lines, $\sigma = 0.11$ ppm. As the sample, is warmed to 80°, the lines coalesce to a single broad resonance. It is likely that this phenomenon would be observed under the conditions in which **1** was studied. Kaplan and Meloy[12] have shown that α-diazoacetaldehyde and several α-diazo ketones and α-diazo esters exist at equilibrium with carbonyl and diazo groups in both *cis* and *trans* configuration. Rotation in these compounds is somewhat hindered so that at low temperatures the rate is slow enough to permit determination of the isomer ratios by nmr spectroscopy. It was found that diazo ketones prefer the *cis* configuration, the *cis* and *trans* forms of diazoesters are present in nearly equal amounts, and α-diazoacetaldehyde is 70% *cis*, 30% *trans* at these temperatures. The conclusion was drawn that steric interactions between the diazo group and alkyl group attached to carbonyl are important in determining the *cis–trans* ratio.

At +50 and +80°, the high-field resonance line of **1** broadens again and moves upfield. We attribute this shift to an increased rate of **1b** *syn*-H $\rightleftharpoons$ **1b** *anti*-H so that appreciable **1b** *anti*-H is present along with **1a** and **1b** *syn*-H. The equilibrium configuration of **1b** *anti*-H is expected to be primarily *trans* on steric grounds as compared to primarily *cis* for **1b** *syn*-H. This expectation is supported by two observations. The fact that the resonance moves further upfield indicates that the *trans* form is becoming important since Kapl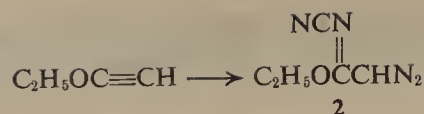an and Meloy[12] found that the *trans* form of all the α-diazocarbonyl compounds which they studied had methine absorption at 0.2–0.5 ppm higher field than the *cis* form. In addition, the slight change in the low-field resonance, which becomes slightly more broad and has a splitting of 2.2 cps compared to 1.5 cps at lower temperature, indicates the presence of the *trans* form in equilibrium with the *cis*. At all temperatures, if we assume as we have that the low-field resonance is C_5–H with coincident absorption, splitting of the low-field resonance will be a weighted average of the forms present. This splitting remains at 1.5–1.7 cps until, near 80°, it opens to ~2.2 cps. Since the *trans* form of **1b** is expected to have a much larger J_{H-H} than the *cis* form (J_{H-H} *trans* for α-diazoacetaldehyde = 7.5 cps; $J_{cis} = 0.3$ cps, $J_{av(70°)}$ = 2.2 cps), we expect the average splitting of the hydrogen to increase with *trans* **1b** content.

Other Cyanogen Azide–Acetylene Adducts. The cyanogen azide adducts of propyne-1, butyne-2, and hexyne-1 have been prepared and show similar spectral features that indicate the triazole–α-diazo-N-cyanoimine tautomerism is present.

The reaction of ethoxyacetylene with cyanogen azide gives ethyl α-diazo-N-cyanoacetimidate (**2**) which appears not to be in equilibrium with the triazole.[14] This material has infrared absorption at 4.55, 4.70, and 6.35 μ and nmr absorption in CD_3CN at τ 4.63 for —CH=N_2

$$\overset{\text{NCN}}{\underset{\parallel}{}}$$
$$C_2H_5OC{\equiv}CH \longrightarrow C_2H_5O\overset{\parallel}{C}CHN_2$$
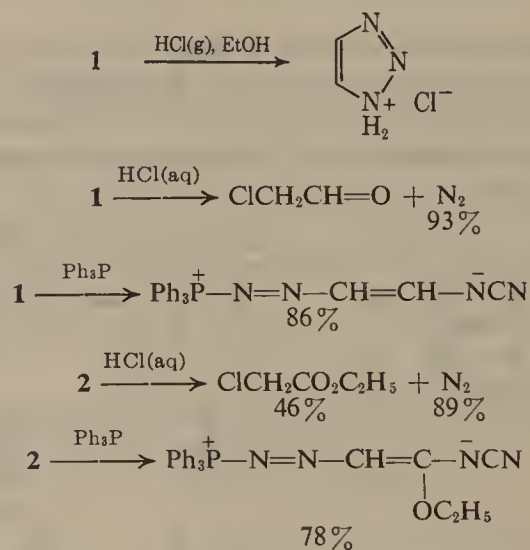$$\mathbf{2}$$

with OC_2H_5 absorption centered at τ 7.63 and 9.00.[15] Neither the infrared nor the nmr spectra are temperature dependent.

The ultraviolet spectrum of **2** resembles that of ethyl diazoacetate: λ_{max} 277 mμ (ϵ 20,300) and 362 mμ (ϵ 55).[16]

Chemistry of the Acetylene Adducts. Perhaps the best evidence for the isomeric structures of **1** and the open-chain compound **2** is provided by hydrolysis experiments. Ethanol solutions of **1** are yellow; however, on passage of HCl gas into the solution, the color is immediately lost and pure 1,2,3-triazole hydrochloride is obtained in 32% yield. It is not known whether this reaction proceeds by rapid ethanolysis of the triazole component or by a rapid shift of **1b** $\rightleftharpoons$ **1a** followed by slow ethanolysis. On addition of **1** to concentrated hydrochloric acid at room temperature, 93% of 1 mole of nitrogen is obtained in 2 hr and chloroacetaldehyde is obtained from the solution.

Reaction of **2** with HCl is more rapid. At room temperature in concentrated HCl after 20 min, 89% of 1 mole of nitrogen is liberated and 46% of ethyl chloroacetate is obtained from the solution.

Both **1** and **2** react with triphenylphosphine without loss of nitrogen to give phosphazine derivatives in high yield.

$$\mathbf{1} \xrightarrow{\text{HCl(g), EtOH}} \text{[triazole]} N_2^+ \, Cl^-$$

$$\mathbf{1} \xrightarrow{\text{HCl(aq)}} ClCH_2CH{=}O + N_2 \atop 93\%$$

$$\mathbf{1} \xrightarrow{Ph_3P} Ph_3\overset{+}{P}{-}N{=}N{-}CH{=}CH{-}\overset{-}{N}CN \atop 86\%$$

$$\mathbf{2} \xrightarrow{\text{HCl(aq)}} ClCH_2CO_2C_2H_5 + N_2 \atop 46\% \quad\quad 89\%$$

$$\mathbf{2} \xrightarrow{Ph_3P} Ph_3\overset{+}{P}{-}N{=}N{-}CH{=}\underset{\underset{OC_2H_5}{|}}{C}{-}\overset{-}{N}CN \atop 78\%$$

Cycloaddition reactions of **2** have been demonstrated with bicyclo[2.2.1]heptene and dimethyl acetylenedicarboxylate. For comparison, the cycloadducts of ethyl diazoacetate (**3**) were also prepared with the above dipolarophiles.[17]

Both **2** and **3** react slowly with bicyclo[2.2.1]heptene in tetrahydrofuran at 65°. After 5 days a 41% yield of crystalline **4a** is obtained from **2**. This compound shows NH absorption (3.00 μ) and two sharp C=N absorption bands at 6.26 and 6.60 μ. Coupled with ultraviolet absorption at 342 mμ (ϵ 13,700), the infrared

(13) M. E. Hermes and F. D. Marsh, *J. Am. Chem. Soc.*, in press.
(14) A similar result from ethoxyacetylene and benzenesulfonyl azide was achieved by P. Grünager and P. Vita Finzi, *Tetrahedron Letters*, 1839 (1963), and P. Grünager, P. V. Finzi, and C. Scotti, *Chem. Ber.*, **98**, 623 (1965).

(15) Reference 12 reports the methine proton in ethyl diazoacetate at τ 5.17.
(16) A. E. Gilman and E. S. Stern, "Electronic Absorption Spectroscopy," Edward Arnold Ltd., London, 1958, p 63, report λ_{max}^{EtOH} 249 mμ (ϵ 10,050), 377.5 mμ (ϵ 16).
(17) Surprisingly, the uncatalyzed addition of ethyl diazoacetate to dimethyl acetylenedicarboxylate and norbornene has not been reported. R. R. Sauers and P. E. Sonnet, *Tetrahedron Letters*, 1029 (1964), report the CuCN-catalyzed addition to bicyclo[2.2.1]heptene with nitrogen loss.

data indicate that **4a** has the conjugated pyrazoline structure shown. Similarly, **3** gives ~50% of **4b**, a high-boiling liquid, after 6 days of reflux in tetrahydrofuran. The infrared spectrum of **4b** shows strong NH absorption at 3.00 μ and C=O and C=N absorptions at 5.90 and 6.22 μ, respectively. Compound **4b** has ultraviolet absorption at 306 mμ (ϵ 6300).

2, X = NCN
3, X = O

4a, X = NCN
b, X = O
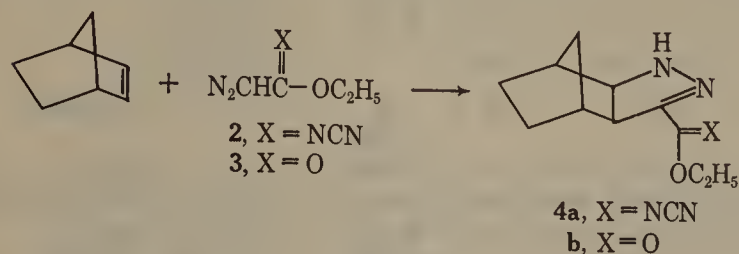
The additions of **2** and **3** to dimethyl acetylenedicarboxylate are somewhat faster than to bicyclo[2.2.1]heptene. A 76% yield of pyrazole **5a** is formed from **2** in 16 hr at 65° and 75% of **5b** is formed in 1 hr from **3**. Both **5a** and **5b** have broad NH absorption near 3.2 μ and carbonyl stretching at 5.70 and 5.80 μ. The nitrile

5a, X = NCN
5b, X = O
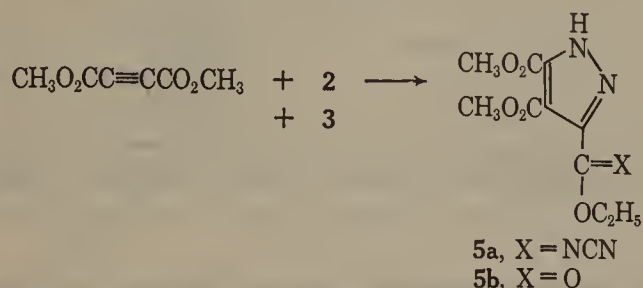
stretching frequency of **5a** is at 4.50 μ. The C=N frequency of the N-cyanoimine is at 6.10 μ and indicates a lack of conjugation with the pyrazole ring since this band is found at 6.25–6.40 μ in **1b**, **2**, and **4a**. Both **5a** and **5b** show pyrazole C=N absorption as a weak band at 6.35 μ.

The ultraviolet spectra of **5a** and **5b** confirm the lack of conjugation with the ring; **5b** shows end absorption only while **5a** has λ_{max}^{EtOH} 215 mμ (ϵ 22,600) with a shoulder at λ_{max}^{EtOH} 250 mμ (ϵ 10,020).

1-Cyanobenzotriazole. The evidence for ring–chain tautomerism of 1-cyano-1,2,3-triazole prompted synthesis of the benzo analog. The reaction of cyanogen azide with benzyne produced from amyl nitrite and anthranilic acid[18] produced very little of the desired triazole; however, 1-cyanobenzotriazole (**6**) was readily prepared by reaction of benzotriazole anion with cyanogen chloride. Triazole **6** is a colorless crystalline material with —C≡N absorption of 4.45 μ. The nmr
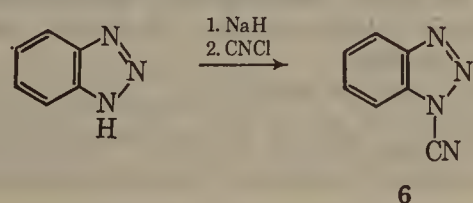

6

spectrum shows that **6** is not the symmetrical 2-cyano compound. Ultraviolet absorption is found at λ_{max}^{EtOH} 253 mμ (ϵ 6620) and 293 mμ (ϵ 3300), and there is a weak band at 435 mμ which is not present in cyclohexane solution. In solution in polar solvents or on melting (mp 73–75°), **6** shows reversible thermochromic behavior. Methanol solutions of **6** are light yellow, and

(18) L. Friedman and F. Logullo, *J. Am. Chem. Soc.*, **85**, 1549 (1963).

the color becomes more intense on heating. The melt of **6** is deep yellow but the color disappears on crystallization.

No other spectral or chemical evidence has been obtained to indicate that color formation might be due to ring opening to the diazo-N-cyanoimine. Nevertheless, this remains an intriguing explanation for the observed color changes.
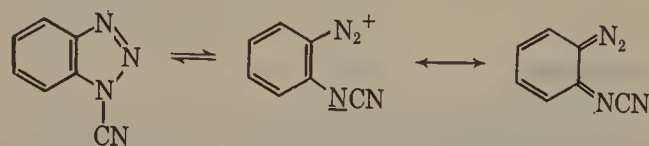
Experimental Section

Warning. Cyanogen azide is a hazardous material. It should be handled only in solution. Concentration of the pure material will lead to violent detonation by heat or shock.

1-Cyanotriazole ⇌ α-Diazo-N-cyanoacetaldehyde Imine (1). An 80-ml Hastelloy pressure tube was charged with 6.5 g (0.10 mole) of sodium azide and 40 ml of acetonitrile. The tube was cooled to −80° and 12 g (0.20 mole) of cyanogen chloride and 10 g (0.40 mole) of acetylene were added. The materials were heated with shaking 12 hr at 45°. The resulting mixture was filtered to remove salts, treated for 10 min at 25° with decolorizing charcoal, and filtered through a bed of Celite. After removal of the acetonitrile at 25° (15 mm) on a rotating evaporator, 7.2 g (77%) of nearly pure **1** remained as a yellow oil. Infrared examination showed only a trace of cyanogen azide (band at 8.0 μ). Sublimation at 20° (0.5 mm) gave pure, crystalline **1**, mp 33°. Spectral data are collected in Table I.

Anal. Calcd for $C_3H_2N_4$: C, 38.3; H, 2.1; N, 59.6. Found: C, 38.4; H, 2.4; N, 59.3.

Methyl-1-cyano-1,2,3-triazole and Isomers. A mixture of 6.5 g (0.10 mole) of sodium azide, 40 ml of acetonitrile, and 12 g (0.30 mole) of propyne was sealed in an 80-ml Hastelloy-lined pressure tube and cooled, and 12 g (0.20 mole) of cyanogen chloride was added. After 20 hr at 45°, the contents were filtered to remove salts, and the solution was treated with decolorizing charcoal and filtered through Celite. Distillation through a short-path molecular-type still gave 6 5 g (60%) of a mixture of 4- and 5-methyl-1-cyano-1,2,3-triazole in equilibrium with open-chain diazo forms, bp 63–72° (pot temperature) (0.5 mm), n^{25}D 1.5142–1.5260.

Anal. Calcd for $C_4H_4N_4$: C, 44.4; H, 3.7; N, 51.9. Found: C, 45.1; H, 4.1; N, 52.0.

The infrared spectrum showed λ_{max}^{liquid} 4.45, 4.62, 4.76, and 6.50 μ, nmr (neat) τ 2.08 (four lines, $J = 1$ cps, 0.27 H), 3.36 (broad, 0.73 H), and 7.86 and 7.96 ($J = 1$ cps, 3 H). The relative weights of the methine peaks show that the methyl group is located 73% at C_5 and 27% at C_4.

4,5-Dimethyl-1-cyano-1,2,3-triazole and Isomer. To a mixture of 8.8 g (0.135 mole) of sodium azide in 35 ml of acetonitrile in an 80-ml Hastelloy-lined tube was added 16 g (0.25 mole) of cyanogen chloride and 14.5 g (0.27 mole) of 2-butyne. After shaking 20 hr at 45°, the contents were filtered and the solvents and excess cyanogen azide removed *without condensation* on a rotating evaporator at room temperature using water-pump vacuum. The residue was distilled through a short-path still at a pot temperature of 50–65° (0.4 mm). The product crystallized on the −15° condenser. A total of 2.2 g (13%) of 4,5-dimethyl-1-cyano-1,2,3-triazole in equilibrium with 2-diazo-1-methylpropylidene cyanamide was obtained.

Anal. Calcd for $C_5H_6N_4$: C, 49.1; H, 5.0; N, 44.9. Found: C, 48.9; H, 5.3; N, 43.6.

The infrared spectrum showed λ_{max}^{liquid} 4.46, 4.56, 4.68, 6.18, and 6.26 μ; nmr: τ 7.82 and 7.98.

Ethyl α-Diazo-N-cyanoiminoacetate (2). A solution of 15 g (0.2 mole) of ethoxyacetylene in 20 ml of carbon tetrachloride was added to 0.1 mole of cyanogen azide in 36 ml of carbon tetrachloride. After 2 hr at 40°, no cyanogen azide remained as determined by gas chromatography. On evaporation of the solvent, 12 g (87%) of crude **2** was obtained. Recrystallization from a mixture of 70 ml of carbon tetrachloride and 100 ml of petroleum ether gave 8.6 g (60%) of pure **2**, mp 49.5–52°.

Anal. Calcd for $C_5H_5N_4O$: C, 43.5; H, 4.4; N, 40.6. Found: C, 43.6; H, 4.5; N, 40.6.

Table III. Reaction of **2** and **3** with Norbornene and Dimethyl Acetylenedicarboxylate

Reactants	Reaction time, hr	Yield, %	Mp, °C	Calcd, %			Found, %			Infrared, μ	Nmr, τ	Ultraviolet, mμ (ε)
				C	H	N	C	H	N			
2 + norbornene	120	41	204–207[a]	62.0	6.9	24.1	62.3	6.4	24.0	3.45 4.55 6.25 6.60	1.9 (1 H) NH 5.7 (3 H) 6.7 (1 H) 7.5 (2 H) 1.2 (9 H)	342 (13,700)
3 + norbornene	144	~50	Oil	63.5	7.7	13.4	63.1	7.4	11.7[b]	3.0 5.90 6.46	...	306 (6300)
2 + CH$_3$O$_2$CC≡CCO$_2$CH$_3$	15	76	172–175[c]	47.1	4.3	20.0	47.0	4.3	19.9	3.3 4.50 5.70 5.77 6.10 6.34	5.6 (1 H) NH 5.7 (2 H) CH$_2$ 6.2 (6 H) CH$_3$O 8.8 (3 H) CH$_3$	215 (22,600) 250 (sh) (10,000)
3 + CH$_3$O$_2$CC≡CCO$_2$CH$_3$	1	75	93–96[d]	47.0	4.7	10.9	46.0	4.8	10.7	3.1 5.70 5.80 6.34	−2.3 (1 H) NH 5.6 (2 H) CH$_2$ 6.1 (1 H) CH$_3$O 8.6 (3 H) CH$_3$	End absorption only

[a] Recrystallized 0.5 g from 20 ml of CH$_3$CN.   [b] Contains some unreacted **3**.   [c] Recrystallized 2.0 g from 20 ml of CH$_3$OH.   [d] Recrystallized from CCl$_4$.

Triazole Hydrochloride from 1. Hydrogen chloride was passed into a solution of 1.60 g (0.017 mole) of **1** in ethanol. An immediate reaction gave a colorless solution. Evaporation of the solvent gave 2.1 g of hygroscopic crystals which gave 0.55 g of triazole hydrochloride on crystallization from acetone [32%, mp 142–145° (lit.[19] 142°)].

Anal. Calcd for C$_3$H$_4$N$_3$Cl: C, 22.8; H, 3.8; N, 39.8. Found: C, 23.2; H, 4.0; N, 39.2.

Chloroacetaldehyde from 1. To 15 ml of concentrated hydrochloric acid was added 2.0 g (0.021 mole) of **1**. After 2 hr at 25°, 500 ml (93%) of nitrogen had evolved. Continuous extraction of the water solution for 16 hr with ether extracted chloroacetaldehyde with gas chromatography retention time identical with that of an authentic sample. The chloroacetaldehyde gave an impure 2,4-dinitrophenylhydrazone derivative, mp 157.5–160°.

Anal. Calcd for C$_8$H$_7$ClN$_4$O$_4$: C, 37.2; H, 2.7. Found: C, 37.9; H, 3.1.

Ethyl Chloroacetate from 2. Treatment of 1.84 g (0.013 mole) of **2** with 20 ml of 2 N hydrochloric acid for 20 min gave 300 ml (89%) of nitrogen and a colorless solution. The solution was extracted twice with ether. The ether was dried and evaporated to give 0.80 g (46%) of ethyl chloroacetate with infrared and nmr spectra and gas chromatographic retention time essentially identical with those of authentic material.

Triphenylphosphine and 1. Mixture of 0.88 g (9.4 mmoles) of **1** and 2.6 g (9.9 mmoles) of triphenylphosphine in 125 ml of ether caused separation of a yellow crystalline adduct without nitrogen evolution. A total of 3.05 g (86%) of [(2-cyanamidovinyl)azo]-triphenylphosphonium hydroxide inner salt was obtained, mp 114–115° dec.

Triphenylphosphine and 2. Reaction of an ether solution of 0.69 g (5 mmoles) of **2** and 1.31 g (5 mmoles) of triphenylphosphine gave 1.55 g (78%) of [(2-cyanamido-2-ethoxyvinyl)azo]triphenyl-phosphonium hydroxide inner salt, mp 130–132°.

Anal. Calcd for C$_{23}$H$_{21}$N$_4$OP: C, 69.2; H, 5.3; N, 14.0. Found: C, 69.1; H, 5.4; N, 13.7.

The ultraviolet spectrum showed $\lambda_{max}^{CH_3CN}$ 268 mμ (ε 5600) and 343 mμ (ε 18,800).

Cycloadducts of 2 and 3 with Norbornene and Dimethyl Acetylenedicarboxylate. Ten millimoles of each reactant were mixed, diluted to 50 ml in tetrahydrofuran, and refluxed, with the results shown in Table III.

1-Cyanobenzo-1,2,3-triazole. A solution of 23.8 g (0.20 mole) of benzotriazole in tetrahydrofuran was added to 9 g of 53.5% sodium hydride in mineral oil (0.2 mole) in 150 ml of tetrahydrofuran. The solution was stirred for 1 hr, then cyanogen chloride (16 g, 0.27 mole) was added over 15 min. The temperature was kept below 40° with cooling.

After 1 hr the solution was filtered and the solvent evaporated to give a partially crystalline oil which was sublimed at 75° (2 μ) to give 19.3 g (67%) of 1-cyanobenzo-1,2,3-triazole, mp 73–75°.

Anal. Calcd for C$_7$H$_4$N$_4$: C, 58.3; H, 2.8; N, 38.9. Found: C, 58.4; H, 3.0; N, 39.4.

The ultraviolet spectra showed λ_{max}^{EtOH} 253 mμ (ε 6620), 293 mμ (ε 3300), and 435 mμ (ε 3.5); $\lambda_{max}^{cyclohexane}$ 249 mμ (ε 7450), 258 mμ (ε 5630), and 293 mμ (ε 3570). The nmr spectrum indicates the presence of little or no 2-cyanobenzo-2,1,3-triazole.

Anal. Calcd for C$_{21}$H$_{17}$N$_4$P: C, 70.4; H, 4.8; N, 15.7. Found: C, 70.8; H, 5.2; N, 15.4.
The spectra showed λ_{max}^{Nujol} 4.60; $\lambda_{max}^{CH_3CN}$ 260 mμ (ε 6100) and 368 mμ (ε 26,800).

(19) R. Hüttel and G. Wetzel, *Ann.*, **593**, 207 (1955).

Mass Spectrometry in Structural and Stereochemical Problems. CXXXII.[1] Electron Impact Induced Alkyl and Aryl Rearrangements in α,β-Unsaturated Cyclic Ketones[2]

R. L. N. Harris,[3a] F. Komitsky, Jr.,[3b] and Carl Djerassi

Contribution from the Department of Chemistry, Stanford University, Stanford, California 94305. Received February 13, 1967

Abstract: The mass spectra of a number of alkyl- and aryl-substituted Δ^2-cyclohexenones and related bicyclic ketones, together with deuterium-labeled analogs, have been measured and the course and scope of an electron impact induced 1,2-alkyl (aryl) rearrangement occurring in these compounds discussed. Ketene elimination and other fragmentation processes in the mass spectra of these compounds are also described.

Electron impact induced alkyl and aryl rearrangements have received wide attention,[4] principally because of their mechanistic interest, but also because of the possible limitations which they may impose on the element map technique for the presentation of mass spectral data. Most of the examples so far documented involve expulsion of a neutral species (*e.g.*, CO, CO_2, SO_2, etc.) from the molecular ion accompanied by a rearrangement of the remainder to give a charged fragment having a different arrangement of carbon atoms from that existing in the original molecule. Authentic 1,2 rearrangements that take place within the molecule without concomitant loss of a neutral fragment are much less commonly observed. One of the first examples of such a rearrangement was observed in the mass spectra of Δ^3-2-octalones bearing a 10-methyl substituent. Thus, a prominent peak ($\Sigma_{40} = 11\%$) in the mass spectrum of I occurs at m/e 69 and has been shown by high resolution and deuterium labeling[5] to correspond to the ion a, which arises by a 1,2 shift of the angular methyl group from C-10 to C-4 prior to fragmentation. Several plausible rationaliza-

I
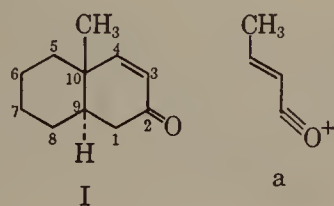
tions have been proposed to account for the formation of the m/e 69 peak (see Scheme I). The principal difference between them is the nature of the neutral (undetectable) fragment produced. However, a distinction can be drawn by considering the structural requirements necessary for the rearrangement to take place. For example, if process A[5] operates, the ketone II should also undergo such a rearrangement. If the concerted 1,2 shifts implicit in process B[6] are involved,

Scheme I
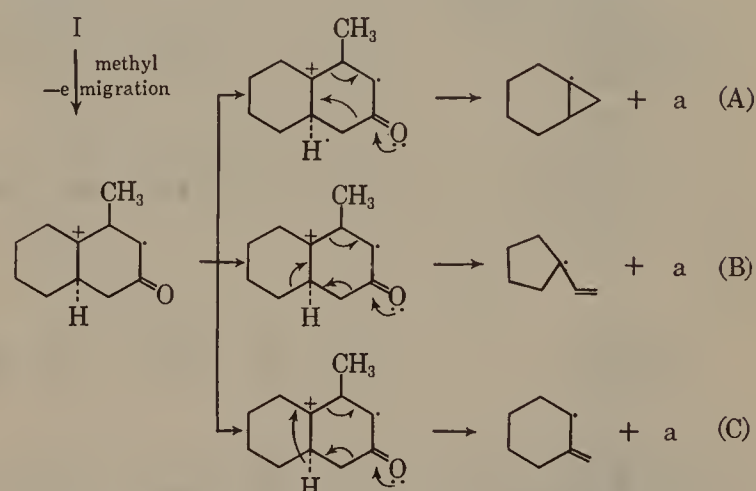
then the ketone III should show the rearrangement even if II did not. If process C[6] were the correct one, then the ketone IV might not be expected to exhibit an m/e 69 peak (a). Accordingly, the appropriate ketones and some deuterated analogs were synthesized and their

II III IV
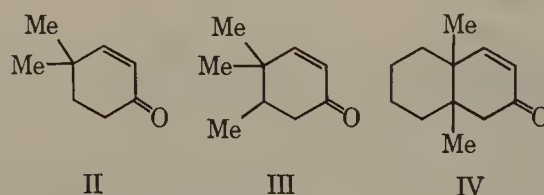
mass spectra measured. The present paper discusses the mechanistic implications of these results; in addition, the scope of the rearrangement has been further delineated by a consideration of the mass spectra of many related α,β-unsaturated cyclic ketones, in which the migrating group is methyl, ethyl, or aryl (see Table I).

Synthesis of the Ketones

Δ^3-Octalones and Related Compounds. Most of these substances have been reported previously (see footnotes to Table I). *trans*-10-d_3-Methyl-2-octalone (Ib) was prepared by the following sequence. The magnesium salt of cyclohexanone cyclohexylimine was alkylated[7] with d_3-methyl iodide to give 2-d_3-methylcyclohexanone. This was condensed[8] with methyl vinyl ketone; the intermediate ketol was dehydrated[8] and the product re-

(1) For paper CXXXI see J. O. Madsen, S.-O. Lawesson, A. M. Duffield, and C. Djerassi, *J. Org. Chem.*, **32**, 2054 (1967).

(2) Financial assistance by the National Institutes of Health (Grants No. AM-04257 and GM-06840) is gratefully acknowledged. The purchase of the Atlas mass spectrometer was made possible through NASA Grant NsG 81-60.

(3) Postdoctoral Research Fellow: (a) 1965–1966; (b) 1964–1965.

(4) For a recent review, see P. Brown and C. Djerassi, *Angew. Chem.*, in press.

(5) F. Komitsky, Jr., J. E. Gurst, and C. Djerassi, *J. Am. Chem. Soc.*, **87**, 1398 (1965).

(6) First proposed by Dr. W. J. Richter (Hoffmann-La Roche, Basel) in a private discussion with one of the authors.

(7) See G. Stork and S. R. Dowd, *J. Am. Chem. Soc.*, **85**, 2178 (1963).

(8) J. A. Marshall and W. I. Fanta, *J. Org. Chem.*, **29**, 2501 (1964).

Table I. Per Cent Total Ionization (Σ_{40}) and Relative Abundance (RA) of Alkyl and Aryl Rearrangement Ions in the Mass Spectra of Δ^2-Cyclohexenones and Related Ketones
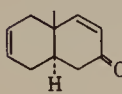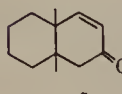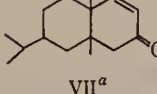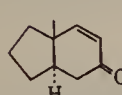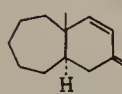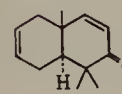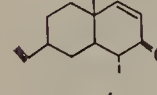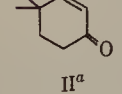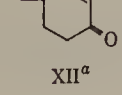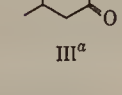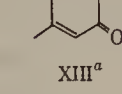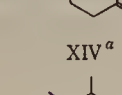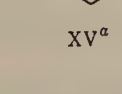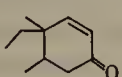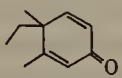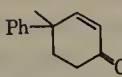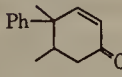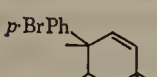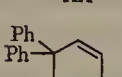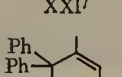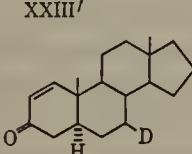
Compound	M^+, 70 ev % Σ_{40}	% RA	M^+, 12 ev % Σ_{40}	% RA	Rearr ion, 70 ev m/e	% Σ_{40}	% RA	Rearr ion, 12 ev % Σ_{40}	% RA	Deuterated analogs	Ref
I[a]	2.6	24	19.2	45	69	11.0	100	6.8	16	1,1,3-d_3 (Ia) m/e 69 → m/e 70 10-d_3-Me (Ib) m/e 69 → m/e 72	b
V[a]	3.14	35			83	9.0	100			1,1,3-d_3 (Va) m/e 83 → m/e 84 4-d_3-Me (Vb) m/e 83 → m/e 87	c
VI[a]	4.2	60			69	5.8	84			4-d_1 (VIa) m/e 69 → m/e 70	b
IV[a]	3.3	47	36	100	69	6.4	92	1.1	3	9-d_3-Me (IVa) m/e 69 unchanged	d
VII[a]	1.6	21	19.8	100	69	7.8	100	2.0	10		d
VIII[a]	2.6	23	18.3	38	69	5.74	51	4.34	9		
IX[a]	1.5	19	13.4	33	69	7.6	96	4.5	11		e
X[a]	1.4	18			69	1.3	17				b
XI[f]	4.1	76			69	3.8	70				g
II[a]	10.9	51	67.6	100	69	1.1	5				
XII[a]	6.3	42	34.9	68	83	0.5	3				
III[a]	5.4	22	34.5	91	69	9.3	38	2.7	7	2,6,6-d_3 (IIIa) m/e 69 → m/e 70 4,4-Di-d_3-Me (IIIb) m/e 69 → m/e 72	
XIII[a]	12.1	84	43.2	100	83						
XIV[a]	3.2	23			69	0.6	4				
					83	0.3	2				
XV[a]	3.5	19			83	0.2	1				
					97						

Table I (*Continued*)

Compound	M+, 70 ev %Σ40	M+, 70 ev %RA	M+, 12 ev %Σ40	M+, 12 ev %RA	Rearr ion, 70 ev m/e	Rearr ion, 70 ev %Σ40	Rearr ion, 70 ev %RA	Rearr ion, 12 ev %Σ40	Rearr ion, 12 ev %RA	Deuterated analogs	Ref
XVI[a]	2.2	11			69	3.4	17			2,6,6-d_3 (XVI)	
					83	4.0	20			m/e 69 → m/e[j] 70	
										m/e 83 → m/e 84	
XVII[a]	6.7	33			69						
					83						
					97						
XVIII[f]	11.2	82	25.9	76	69	0.1	1				
					131	0.4	3	0.3	0.5		
XIX[a]	6.2	32	35.8	100	69	0.8	4			2,6,6-d_3 (XIXa)	
					131	8.0	41	14.7	41	m/e 69 → m/e 70	
										m/e 131 → m/e 132	
XX[f]	6.7	31	25.7	100	69	0.6	3	0.3	1		
					209	7.7	36	17	66		
					211						
XXI[f]	2.0	16	8.1	16	131	0.3	2				h
XXII[f]	10.4	100			145	0.1	1				
XXIII[f]	7.5	36	20	100	69	2.7	13	1.6	8	2,4,6,6-d_4 (XXIIIa)	
										m/e 69 → m/e 70	
XXIV[f]	1.5	28			69	1.2	23				i

[a] Mass spectrum measured on Atlas CH-4 spectrometer. [b] C. Djerassi and D. Marshall, *J. Am. Chem. Soc.*, **80**, 3986 (1958). [c] L. H. Zalkow, F. X. Markley, and C. Djerassi, *ibid.*, **82**, 6354 (1960). [d] The authors wish to thank Professor J. A. Marshall for a generous gift of this compound; see J. A. Marshall, W. I. Fanta, and H. Roebke, *J. Org. Chem.*, **31**, 1016 (1966). [e] C. Djerassi and J. E. Gurst, *J. Am. Chem. Soc.*, **86**, 1755 (1964). [f] Mass spectrum measured on AEI MS-9 mass spectrometer using direct inlet method. [g] The authors wish to thank Professor T. Nozoe for a generous gift of this compound; see T. Nozoe, Y. S. Cheng, and T. Toda, *Tetrahedron Letters*, 3663 (1966). [h] H. E. Zimmerman and D. I. Schuster, *J. Am. Chem. Soc.*, **84**, 4527 (1962). [i] R. H. Shapiro and C. Djerassi, *ibid.*, **86**, 2865 (1964).

duced with lithium in liquid ammonia.[9] Oxidation[10] of the resulting saturated alcohol gave the corresponding decalone which was brominated (pyridinium perbromide in acetic acid) and dehydrobrominated (calcium carbonate in N,N-dimethylacetamide[11]) to give the required Δ^3-10-d_3-methyloctalone. cis-9-d_3-Methyl-10-methyl-Δ^3-2-octalone (IVa) was prepared in a manner analogous to that used for the 1-methyl compound.[9] The deuterated ketones Ia and Va were obtained by refluxing the appropriate ketone with sodium in methanol-d_1 and heavy water.[12]

(9) See G. Stork and S. D. Darling, *J. Am. Chem. Soc.*, **86**, 1761 (1964).
(10) K. Bowden, I. M. Heilbron, E. R. H. Jones, and B. C. L. Weedon, *J. Chem. Soc.*, 39 (1946).
(11) G. F. H. Green and A. G. Long, *ibid.*, 2532 (1961).
(12) R. H. Shapiro, J. M. Wilson, and C. Djerassi, *Steroids*, **1**, 1 (1963).

4,4-Disubstituted Cyclohexenones. Two general methods of synthesis were employed. The first involved base-catalyzed condensation of methyl vinyl ketone with the appropriately substituted aldehyde and is satisfactory only when either or both C-4 substituents are aryl (XVIII–XXII). 4,4-Dialkylcyclohexenones (II and XIV) were synthesized by alkylation–cyclization of the appropriate aldehyde enamine with methyl vinyl ketone.[13]

4,4,5-Trisubstituted Cyclohexenones. 4,5-Dimethyl-4-aryl-Δ^2-cyclohexenones (XIX and XX) were prepared by condensing the appropriate aldehyde with pent-2-en-3-one. The trialkylcyclohexenones (III and XVI) were obtained by 1,3 addition of methylmagnesium iodide to the corresponding 4,4-dialkylcyclohexenone, fol-

(13) G. Stork, A. Brizzolara, H. Landesman, J. Smuszkovicz, and R. Terrell, *J. Am. Chem. Soc.*, **85**, 207 (1963).

lowed by bromination and dehydrobromination. This second route was complicated by the formation of the 1,2-addition product in the first step and of both isomeric α,β-unsaturated ketones (e.g., III and XII) and the corresponding dienone (e.g., XIII) in the second step. In most instances, however, separation of these compounds was accomplished readily by gas–liquid partition chromatography.

Deuterated Cyclohexenones. The hydrogen atoms α to the carbonyl group were exchanged with deuterium by refluxing a solution of the ketone in methanol-d_1 and heavy water containing a trace of potassium carbonate. The synthesis of 4,4-di-(d_3-methyl)-5-methyl-Δ^2-cyclohexenone (IIIb) was achieved as follows (Scheme II).

Scheme II

IIIb
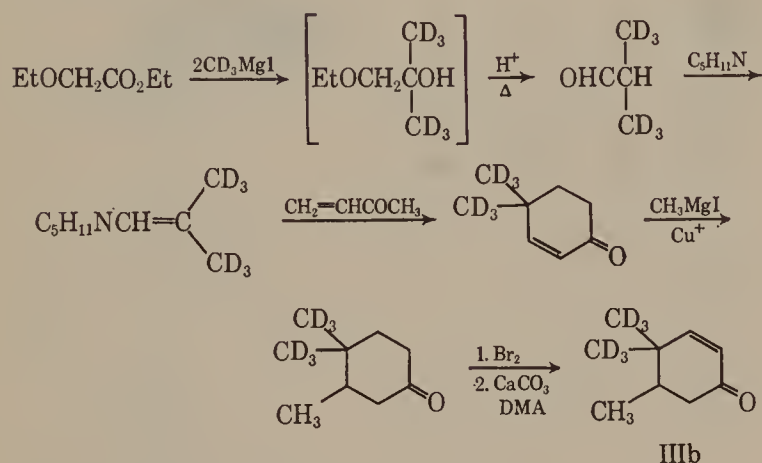
Ethyl ethoxyacetate was treated with 2 equiv of d_3-methylmagnesium iodide and the resulting propanediol monoethyl ether heated with aqueous sulfuric acid. Steam distillation gave the labeled aldehyde which was immediately condensed with piperidine in ether in the presence of anhydrous potassium carbonate[14] to afford the enamine in which there was no scrambling of the deuterium as shown by nmr and mass spectrometry. The desired ketone IIIb was prepared from this enamine by the procedure used for the undeuterated analog.

Discussion of the Mass Spectra

The Rearrangement Ion a. The main feature of interest in the mass spectra of the α,β-unsaturated cyclic ketones is the occurrence of the rearrangement ion a, and the discussion will first be concerned with it. The intensity of fragment a in the mass spectra of the ketones studied is recorded in Table I both as per cent total ionization (% $\Sigma_{40}M^+$) and per cent abundance relative to the most intense peak (% RA). The intensity of the molecular ion is included for comparison. In many cases the spectra were measured at low voltage (12 ev) as well as at the customary 70 ev.

High-resolution mass spectral measurements confirmed the elemental composition of the rearrangement ion in all relevant examples. Furthermore, the inclusion of the implicated carbon atoms in the rearrangement ion a was substantiated in most cases by deuterium labeling, as shown in Table I. The migration of the phenyl group in XIX was confirmed by labeling this group with a p-bromine atom (see XX). The aryl rearrangement ion shifted from m/e 131 to m/e 209–211

as would be expected. All the bicyclic ketones show the rearrangement ion in their mass spectra; in fact, the ion is in most cases of greater than 90% relative abundance.

Significantly, substitution of the C-9 hydrogen atom by a methyl group in the Δ^3-2-octalones (IV and VII) does not restrict the migration of the C-10 methyl substituent. In view of this observation, process C in Scheme I, which requires the migration of a secondary hydrogen atom from C-9, is either not operative or at least cannot be the only process by which such methyl rearrangements take place. The deuterated analog IVa still shows the rearrangement ion at m/e 69, indicating that the d_3-methyl group at C-9 is not part of this charged species. As reported previously,[5] the presence of a double bond (cf. VI) in ring B of the bicyclic ketones has no effect on the rearrangement process. Furthermore, a consideration of the mass spectra of ketones I, VIII, and IX reveals that the size of ring B also has very little effect on the abundance of the rearrangement ion. All the observations discussed so far can be accommodated by either process A or B in Scheme I.

However, only one of these reaction sequences offers a rationale for the mass spectra of the monocyclic ketones and their deuterated derivatives listed in Table I. Thus, ions due to the rearrangement of methyl, ethyl, or phenyl substituents (m/e 69, 83, and 131, respectively) are almost absent in the mass spectra of ketones II, XIV, and XVIII, whereas in the C-5-methyl homologs III, XVI, and XIX, these rearrangement ions now account for $\Sigma_{40} = 7.3$–9.3% and thus are of the same order of abundance as that observed for rearrangement ions in the octalone series. Therefore alkyl substitution at C-5 in the cyclohexenones appears to be necessary for the rearrangement ion a to be produced. This corresponds to one of the sites of attachment of ring B in the octalone series. Clearly, the results implicate the C-5 substituent in the rearrangement process, and of the three reaction paths proposed so far, only the second (B in Scheme I) remains valid. A more recent variant[15] of B for the course of the rearrangement process is shown in Scheme III. In this sequence the

Scheme III
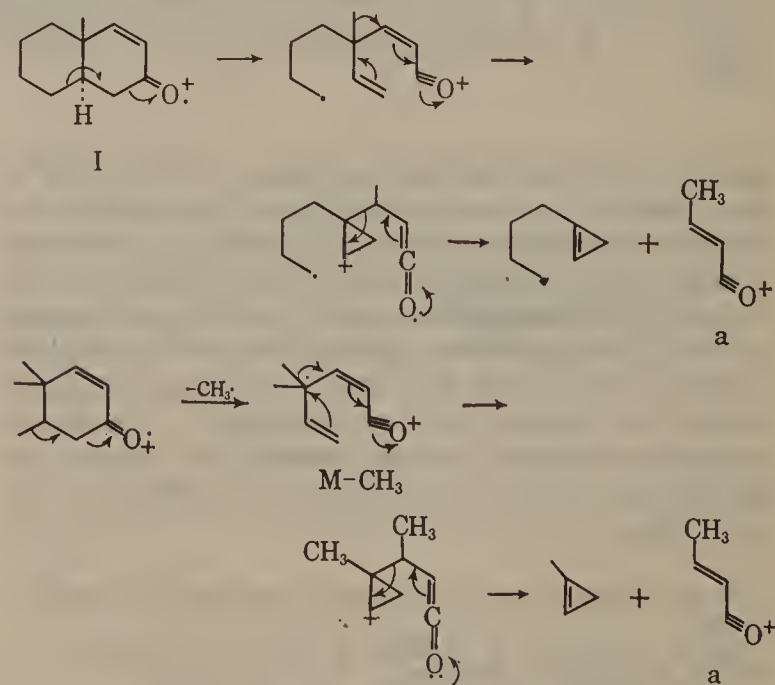
(14) C. Mannich and H. Davidsen, *Ber.*, **69**, 2106 (1936).

(15) Suggested by Drs. P. Brown and M. M. Green in our laboratory.

molecular ion is depicted with charge localization on oxygen rather than the carbon–carbon double bond. Again, the C-5 substituent is involved, and in the octalone series there is no way in which this proposal can be distinguished from that embodied in B of Scheme I.

In the cyclohexenones, however, preliminary cleavage as depicted in Scheme III will result in the generation of an intermediate M − CH$_3$ fragment, and the rearrangement ion would be formally derived from this species in a secondary process. A careful investigation of the relevant spectra reveals no metastable ions to support this hypothesis, whereas the concerted nature of the rearrangement process from molecular ion to phenyl rearrangement ion (m/e 131) in the mass spectrum of XIX is substantiated by a prominent metastable peak at m/e 85.8. It should be noted, however, that in the d_6-labeled ketone IIIb ejection of the C-5 methyl group occurs to a greater extent than loss of one of the allylically activated d_3-methyl substituents, and so fragmentation, as depicted in the first step of Scheme III, is not an unreasonable process.

It has been established that a C-5 substituent is necessary for the rearrangement ion to be produced. Variation of substituents at C-4 has shown that both alkyl and aryl groups are able to migrate. To further define the scope of the rearrangement the mass spectra of the ketone XXIII and its deuterated d_4-analog XXIIIa were measured, and the results (Table I) show that both the C-4 hydrogen atom and the C-4 methyl group undergo migration giving rearrangement ions at m/e 55 (m/e 57 in XXIIIa) and m/e 69 (m/e 70 in XXIIIa), respectively. Migration of a hydrogen atom ($\Sigma_{40} = 8.7\%$) is preferred over that of the methyl group ($\Sigma_{40} = 2.7\%$).

The mass spectra of many of the ketones were also run at low voltages so that favored, primary fragmentations could be distinguished from subsequent or higher energy processes. The results (Table I) do not permit any generalization, but the large increase in the per cent total ionization of the phenyl rearrangement ion (m/e 131) in the 12-ev mass spectrum of XIX is worthy of note. This result suggests that the aryl rearrangement is an energetically favorable primary fragmentation process and corroborates the evidence from the metastable peak described above. In conclusion, therefore, it may be stated that the 1,2 rearrangement ion in the mass spectra of 4,5-disubstituted and 4,4,5-trisubstituted Δ^2-cyclohexenones and related bicyclic ketones is generated in a process involving participation of the C-5 alkyl substituent, and that it is most probably of a concerted nature from the molecular ion to the rearrangement ion.

The mass spectra of a number of other alkyl- and aryl-substituted cyclohexenones were measured (see Table I), and it was found that the rearrangement ion occurred to a significant extent only when the basic 4,5-disubstitution pattern was present in the molecule. For example, XII, although isomeric with III, exhibits only a minor peak at m/e 69. The mass spectra of two cyclohexadienones (XIII and XVII), obtained as side products in our synthetic work, were also measured and no rearrangement ion was observed.

Of considerable interest is the question of relative migratory aptitudes in electron impact promoted alkyl and aryl migrations. It is not surprising that in the
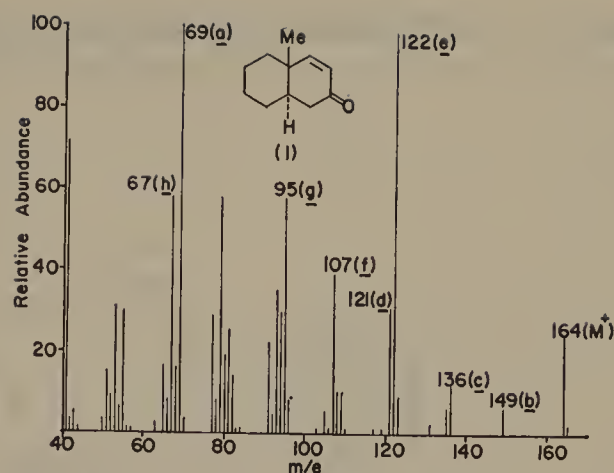
Figure 1. Mass spectrum of *trans*-10-methyl-Δ^3-2-octalone (I); see Scheme IV.

mass spectrum of XIX, the phenyl rearrangement ion (m/e 131) is much more intense than the methyl rearrangement ion (m/e 69), whereas in the spectrum of XVI, both methyl and ethyl migrations occur to a similar extent. However, a quantitative comparison of migratory aptitudes cannot be inferred from a comparison of rearrangement ion intensities in this class of compounds because of the possible influence of stereochemical factors on the rearrangement process and the different subsequent fragmentations of the respective rearrangement ions.

Other Principal Fragmentation Processes

The mass spectra of several of the ketones will be considered in detail to define the nature of other important fragmentation processes in cyclic α,β-unsaturated ketones.

trans-10-Methyl-Δ^3-2-octalone (I). Some aspects of the mass spectrum (Figure 1) of this compound have been discussed previously.[16] However, further information is now available and a more complete evaluation of its spectrum is possible. The principal fragmentation processes are outlined in Scheme IV. The composition of the ions shown was established by high-resolution mass measurements and in some instances metastable ions (shown by asterisks) support the postulated fragmentation pathways. Further evidence for these processes has been obtained from consideration of the mass spectra of the two deuterated derivatives Ia and Ib (see Table II).

cis-9,10-Dimethyl-Δ^3-2-octalone (IV). The mass spectrum (Figure 2) is similar to that of the octalone I; again ejection of carbon monoxide, a methyl radical, and ketene are important although the base peak is now at m/e 95 (g). At 12 ev the only significant fragmentation is loss of ketene.

4,4,5-Trimethyl-Δ^2-cyclohexenone (III). The mass spectrum (Figure 3) shows clearly that again the same principal fragmentation pathways operate. Ions resulting from elimination of carbon monoxide, methyl radical, and ketene are evident, and the ion e produced by expulsion of propene contributes substantially (Scheme V) to the base peak (m/e 96). This cleavage is analogous to that leading to the peak at m/e 95 in the octalone series. The most significant fragmentation

(16) H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Interpretation of Mass Spectra of Organic Compounds," Holden-Day, Inc., San Francisco, Calif., 1964, p 157.

Scheme IV.[a]   Major Fragmentation Pathways of *trans*-10-Methyl-Δ³-2-octalone (I)

I, *m/e* 164

c, *m/e* 136

b, *m/e* 149

d, *m/e* 121

e, *m/e* 122

f, *m/e* 107

a, *m/e* 69   h, *m/e* 67   g, *m/e* 95
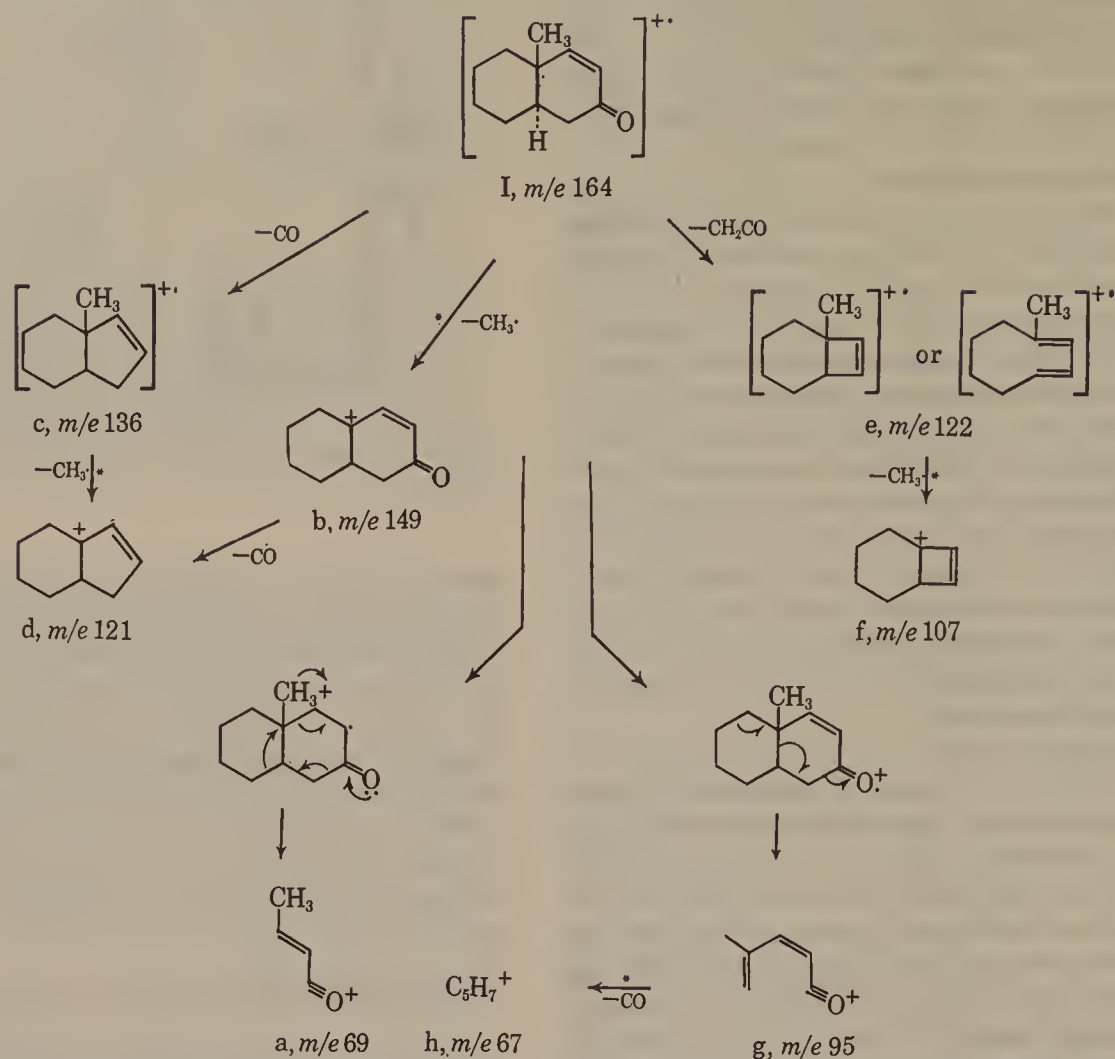
[a] Many of the cyclic structures in this (*e.g.*, ions c, e, and f) and subsequent schemes can also be written in an open form [see B. J. Millard and D. F. Shaw, *J. Chem. Soc., Sect. B.*, 664 (1966)]. The cyclic structures are used here solely for the sake of convenience.

Table II.   *m/e* Values for Various Fragment Ions of *trans*-10-Methyl-Δ³-2-octalone (I) and Deuterated Derivatives

Compound	b	c	e	d	g	a	h
I	149	136	122	121	95	69	67
Ia	152	139	123	124	96	70	68
Ib	149	139	125	121	98	72	70

[a] See Scheme IV.

processes are shown in Scheme IV and supporting evidence from deuteration studies is listed in Table III. These studies show that loss of a methyl radical occurs both from C-4 (b) and C-5 (b′) and both resulting ions subsequently expel carbon monoxide to give an ion (d) of mass 95. The mass spectrum of isophorone (XXV) has recently been published[17] and differs significantly from that of its isomer III. Although ions resulting from loss of carbon monoxide, methyl radical,

(17) J. H. Bowie, *Australian J. Chem.*, **19**, 1619 (1966).

and isobutene (*cf.* propene in III) are abundant, loss of ketene is a very minor process (*vide infra*).

XXV
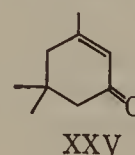
4,4-Dimethyl-Δ²-cyclohexenone (II). The mass spectrum (Figure 4) resembles that of the trimethyl homolog III. All principal peaks are derived by loss of ethylene, ketene, or carbon monoxide and/or a methyl radical. The rearrangement ion (*m/e* 69) is now insignificant. The mass spectrum of II differs in one important respect from that published for Δ²-cyclohexenone;[17] namely, in the former loss of ketene furnishes the base peak, whereas in the latter the M − 42 ion is only of 3% relative abundance.

4,5-Dimethyl-4-phenyl-Δ²-cyclohexenone (XIX). The mass spectrum (Figure 5) resembles that of the ketone III; loss of ketene, propene, and carbon monoxide followed by loss of a methyl radical are important processes. Migration of the C-4 methyl group (giving the rearrangement ion a, *m/e* 69) is now overshadowed by rearrangement of the C-4 phenyl substituent, leading to an analogous ion of mass 131.

Loss of Ketene. One of the more prominent modes of fragmentation of many of the Δ²-cyclohexenones studied is the elimination of ketene. This process has been observed already in steroidal α,β-unsaturated

Table III. *m/e* Values for Various Fragment Ions of 4,4,5-Trimethyl-Δ²-cyclohexenone (III) and Deuterated Derivatives

Compound	b, b'	c	e, f	d	g, h	a	i	j
III	123	110	96	95	81	69	68	53
IIIa	126	113	97	98	82	70	69	54
IIIb	126, 129	116	102	98, 101	84	72	74	56

m/e values of fragment ions[a]

[a] See Scheme V.

Scheme V. Major Fragmentation Pathways of 4,4,5-Trimethyl-Δ²-cyclohexenone (III)

Table IV. Per Cent Total Ionization of Ions Produced by Ketene and Propene Elimination from Δ²-Cyclohexenones

Compound	Loss of ketene (% Σ_{40})	Loss of propene (% Σ_{40})
	0.27	1.53
XXIII	4.2	16.7
II	20.1	...
III	6.8	12.7
XIX	9.7	14.7
I	10.3	~1
IV	6.2	~1

ketones (*e.g.*, XXVII)[18] and occurs in the mass spectra of all the ketones in the present study. It was surprising, therefore, to find that elimination of ketene from Δ²-cyclohexenone itself proceeds only to a negligible extent, an observation first reported by Bowie[17] and confirmed in our own laboratories. Table IV lists the per cent total ionization of the species produced by ketene elimination (*i.e.*, the M − 42 ion) from several Δ²-cyclohexenones. It should be noted that 5-methyl-substituted Δ²-cyclohexenones also eliminate propene, giving rise to an oxygen-containing M − 42 species and high-resolution mass measurements were necessary, therefore, to distinguish this process from ketene elimination (see Table IV).

From the table it is clear that alkyl or aryl substitution at C-4 is necessary for ketene elimination to occur. Recently Egger has shown[19] that ketene elimination

from steroidal α,β-unsaturated ketones may depend on the stereochemistry of the A/B ring junction. For example, in the spectrum of Δ¹-5α-androsten-17β-ol-3-one (XXVII) the M − 42 peak is of 56% relative

XXVII

abundance (the molecular ion being responsible for the base peak), whereas in the 5β isomer loss of ketene is negligible. Similarly, in the corresponding 17-keto

(18) See footnote *i*, Table I.
(19) H. Egger, *Monatsh.*, **97**, 1201 (1966).

Figure 2. Mass spectrum of cis-9,10-dimethyl-Δ³-2-octalone (IV). The ions of mass 163, 150, 136, and 135 are analogs of ions b, c, e, and d in Scheme IV. Ions a, h, and g are identical with those depicted in Scheme IV

Figure 4. Mass spectrum of 4,4-dimethyl-Δ²-cyclohexenone (II). The ions of mass m/e 109, 96, 82, 81, and 67 are analogs of ions b, c, e, d, and g in Scheme V. Ions of mass 96, 81, 68, and 53 correspond to ions f, g, i, and j of Scheme V.

Figure 3. Mass spectrum of 4,4,5-trimethyl-Δ²-cyclohexenone (III); see Scheme V.

Figure 5. Mass spectrum of 4,5-dimethyl-4-phenyl-Δ²-cyclohexenone (XIX). Ions of mass 185, 172, 158, 157, 143, 130, and 115 are analogs of ions b, c, e–f, d, g–h, i, and j in Scheme V. Ions of mass 69 and 131 are the methyl rearrangement ion a and the corresponding phenyl rearrangement product, respectively.

steroids the 5α isomer has a prominent M − 42 peak (84% relative abundance), whereas the 5β isomer exhibits a very weak M − 42 peak (4% relative abundance). A possible rationale for these observations is outlined in Scheme VI. Direct fission of the bond connecting the vinylic carbon to the carbonyl group is an unlikely process and almost certainly implies that a prior rearrangement of the molecular ion a occurs. Thus, rearrangement of a to b, with its highly substituted ionized double bond, provides a cyclobutanone species from which ketene elimination would be a most favorable process (b → c). The resulting M − 42 ion c is a resonance-stabilized ionized butadiene and may also be visualized as the ionized cyclobutene form c'. Such a concerted sequence will probably only operate when there is a suitable driving force for rearrangement of the molecular ion a to species b, such as alkyl or aryl substitution at C-4. This would explain the failure of Δ²-cyclohexenone itself to eliminate ketene on electron impact.[20] The failure of the 5β- (but not 5α-) Δ¹-3-keto steroids[19] to undergo ketene elimination may be associated with the "frozen" conformation of cis-octalones in steroidal systems. By comparison, the flexible cis-octalone (IV) shows an intense peak in its mass spectrum (see Table IV) corresponding to the loss of ketene, possibly because it may assume the proper

(20) After completion of our manuscript, Professor A. L. Burlingame (University of California) sent us a copy of a paper by A. L. Burlingame, C. Fenselau, W. J. Richter, W. G. Dauben, G. W. Shaffer, and N. D. Vietmeyer [J. Am. Chem. Soc., 89, 3346 (1967)] in which the same results with a different interpretation are recorded.

conformation required for the initial rearrangement (a → b).

Scheme VI
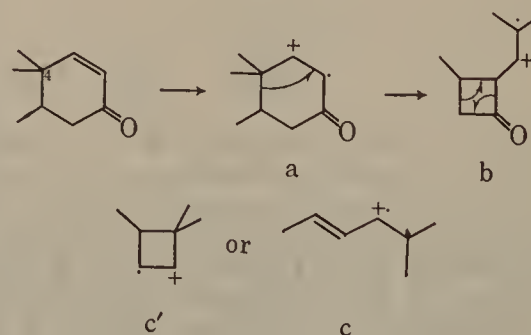
Experimental Section[21]

trans-10-d₃-Methyl-Δ³-2-octalone (Ib). A solution of 0.7 M methylmagnesium iodide in tetrahydrofuran (138 ml) was stirred

under nitrogen and a solution of cyclohexanone cyclohexylimine (16.94 g) in tetrahydrofuran (50 ml) was added slowly during 20 min while the solution was brought to reflux. The mixture was heated under reflux for 2 hr and cooled to 0° and a solution of 89% isotopically pure d_3-methyl iodide (13.4 g) in ether (30 ml) added dropwise with stirring over a period of 20 min. The mixture was heated for 9 hr, cooled, and treated with water (10 ml) followed by 5% hydrochloric acid (30 ml). After stirring for 30 min, 10% hydrochloric acid (25 ml) was added and the mixture stirred a further 20 min, then poured into a saturated solution of sodium chloride (75 ml). The product was extracted into ether (four 50-ml portions); the combined ether extracts were washed with saturated aqueous sodium bicarbonate solution and dried over anhydrous magnesium sulfate. The ether was removed and 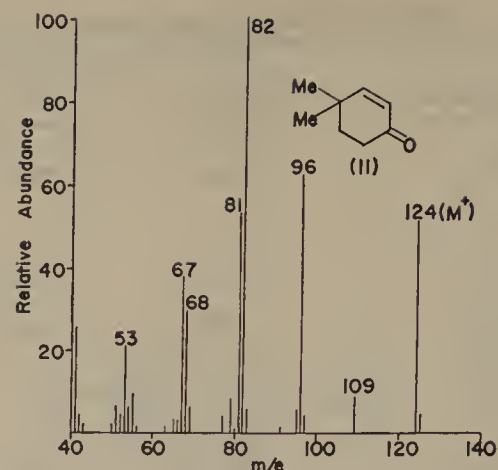the residue distilled through a short Vigreux column. The fraction bp 160–164° (8.87 g, 82%) was collected and shown by infrared and mass spectra and glpc (10-ft free fatty acid phase column, 150°) to be pure 2-d_3-methylcyclohexanone.

The labeled cyclohexanone (8.71 g) and 3 N ethanolic sodium ethoxide solution (0.47 ml) was stirred under nitrogen and cooled to −10°. Freshly distilled methyl vinyl ketone (5.55 g) was added during 6 hr at this temperature and the thick mixture kept at −10° a further 6 hr. Ether was added; the mixture was washed with brine and the organic layer dried over anhydrous magnesium sulfate. The ether was slowly evaporated on a steam bath, the level being maintained by the addition of hexane. A small amount of polymeric material precipitated and was removed by filtration. On cooling the filtrate 9-hydroxy-10-d_3-methyl-2-decalone crystallized as colorless needles, mp 120–121°. The identity of the ketol was confirmed by comparison of its mass spectrum with that of the authentic unlabeled analog.[8] The crude ketol was heated under reflux with a solution of potassium hydroxide (10.3 g) in water (100 ml) and the mixture steam distilled until the distillate was clear. The distillate (1 l.) was saturated with sodium chloride and extracted with ether (four 250-ml portions) and the ether extract washed with brine and dried over anhydrous magnesium sulfate. The residue on removal of the ether was purified by chromatography on silica gel (100 g/g of product), eluting with successive 100-ml portions of 1:1 hexane–benzene, benzene, 5% ether in benzene, 10% ether in benzene, and finally 300 ml of 10% ether in benzene. The latter solvent eluted the required octalone which was used directly in the next step.

The octalone (1.88 g) in ether (50 ml) was added dropwise during 20 min to a solution of lithium (1 g) in liquid ammonia (100 ml) cooled in Dry Ice. After the addition was complete, the cooling bath was removed; the solution was stirred for 80 min as the ammonia evaporated, and methanol (15 ml) in ether (75 ml) was then added, followed by water (75 ml). The mixture was stirred until clear and extracted with ether (three 100-ml portions). The ether extracts were combined, dried over anhydrous magnesium sulfate, and evaporated. The residue was dissolved in acetone (60 ml), treated with a slight excess of Jones reagent,[10] and poured into saturated aqueous bicarbonate solution and the product extracted into ether. The ether extract was dried and evaporated and the residue bulb-distilled to give *trans*-10-d_3-methyl-2-decalone (1.1 g).

A solution of the decalone (1.1 g) in acetic acid (20 ml) was stirred at room temperature, and pyridinium hydrobromide perbromide (2.12 g) was added in portions during 20 min. The solution was stirred a further 30 min, then poured into water and the precipitated bromo ketone collected and recrystallized from acetone–water as colorless needles, mp 135–137° (1.14 g). The recrystallized bromo ketone was dissolved in N,N-dimethylacetamide (5 ml) and added to a suspension of calcium carbonate (1.75 g) in N,N-dimethylacetamide (15 ml). The mixture was heated under reflux for 15 min, then poured into water (70 ml) containing hydrochloric acid (10%; 30 ml). The mixture was extracted with ether (three 25-ml portions); the ether extract was washed successively with 10% hydrochloric acid, saturated aqueous sodium bicarbonate solution, and brine and dried over anhydrous magnesium carbonate and the ether removed. The residual oil was purified by glpc (10-ft 5% diethylene glycol succinate on 60–80 Chromosorb W, 140°) to give a small amount of recovered decalone and the required *trans*-10-d_3-methyl-Δ³-2-octalone as shown by mass (Figure 1) and ultraviolet (λ_{max} 227 mμ) spectra.

trans-8-Methyl-Δ⁶-hydrinden-5-one (VIII). A solution of *trans*-8-methylhydrindan-5-one[22] (0.1 g) in glacial acetic acid (3.5 ml) was stirred at room temperature and a solution of bromine in acetic acid (10% v/v; 0.36 ml, 1 mole equiv) was added during 5 min. The mixture was stirred a further 5 min and poured into water, and the bromo ketone extracted into ether (two 10-ml portions). The ethereal extract was washed with water (10 ml) and saturated aqueous sodium bicarbonate solution (10 ml) and dried over anhydrous magnesium sulfate. The ether was removed and the crude product heated under reflux for 30 min with N,N-dimethylacetamide (5 ml) containing a suspension of powdered calcium carbonate (0.1 g). After filtration, the mixture was poured into water and the product extracted with ether (two 10-ml portions). The ethereal extracts were combined, washed with water (two 15-ml portions), and dried. Removal of the ether gave the hydrindenone as an oil which was purified by glpc (5-ft 10% SE 30 on 60–80 Chromosorb W; 200°). The nmr spectrum (CDCl₃ solution) showed a quadruplet centered at δ 6.5 (J = 9 cps) due to the two vinylic protons at C-6 and C-7. *Anal.* Calcd for $C_{10}H_{14}O$: C, 79.95; H, 9.39; mol wt, 150. Found: C, 80.29; H, 9.19; mol wt (mass spectroscopy), 150.

cis-10-Methyl-9-d_3-methyl-Δ³-2-octalone (IVa). This ketone was prepared by 1,4 addition of d_3-methylmagnesium iodide to 10-methyl-Δ¹⁽⁹⁾-2-octalone,[23] followed by bromination and dehydrobromination of the resulting decalone by the procedure used for the unlabeled analog.[23]

4,4-Dimethyl-Δ²-cyclohexenone (II). The enamine from isobutyraldehyde and piperidine was prepared by the general method of Mannich and Davidsen[14] and was obtained as colorless oil, bp 77–78° (28 mm). This enamine (11 g) was stirred under nitrogen at 0° and redistilled methyl vinyl ketone (6.1 g) added dropwise during 5 min. The mixture was stirred 4 days at room temperature under nitrogen, dissolved in 15% aqueous hydrochloric acid (85 ml), left at room temperature for 24 hr, and finally heated on a steam bath for 1 hr. The cooled mixture was extracted with ether (two 50-ml portions), and the extracts were combined, washed with water (two 25-ml portions), and dried over anhydrous magnesium sulfate. After removal of the ether the residual oil was distilled under reduced pressure to give 4,4-dimethyl-Δ²-cyclohexenone (II) as a colorless oil (6.8 g, 69%), bp 81–83° (26 mm) [lit.[24] 72.5–73.5° (20 mm)]. *Anal.* Calcd for $C_8H_{12}O$: C, 77.37; H, 9.74; mol wt, 124. Found: C, 77.51; H, 9.76; mol wt (mass spectroscopy), 124.

4,4,5-Trimethyl-Δ²-cyclohexenone (III). 4,4-Dimethyl-Δ²-cyclohexenone (0.7 g) and copper acetate monohydrate (0.214 g) were dissolved in anhydrous tetrahydrofuran (20 ml) and stirred under nitrogen in a Dry Ice–acetone bath while (15 min) the Grignard reagent from methyl iodide (1.0 ml) and magnesium (0.4 g) in ether (20 ml) was added dropwise. The mixture was allowed to warm to room temperature, left for 1 hr, heated under reflux for 30 min, and finally decomposed by the addition of excess saturated aqueous ammonium chloride solution. The product was taken into ether (two 15-ml portions), and the combined ether layers were washed with water (two 15-ml portions) and dried (anhydrous magnesium sulfate). The infrared spectrum of the crude product showed that both 1,2- and 1,4-addition products (*i.e.*, allylic alcohol and saturated ketone) were present. These were separated by preparative glpc (10-ft 20% Carbowax 20M on 60–80 Chromosorb W, 150°). The first fraction (15%) was shown to be the allylic alcohol (infrared spectrum) and was not characterized further. The second fraction (85%) was shown to be 4,4,5-trimethylcyclohexanone (γ_{max}^{film} 5.80 μ). *Anal.* Calcd for $C_9H_{16}O$: C, 77.09; H, 11.50; mol wt, 140. Found: C, 76.83; H, 11.44; mol wt (mass spectroscopy), 140.

The above saturated ketone (0.5 g) was dissolved in glacial acetic acid (10 ml), protected from moisture, and stirred during the dropwise addition of a solution of bromine in acetic acid (10% w/v, 5.8 ml). The mixture was stirred a further 10 min and poured into water and the bromo ketone taken into ether (two 50-ml portions). The ethereal extracts were combined, washed with water (50 ml) and saturated aqueous sodium bicarbonate solution (50 ml), and dried (anhydrous magnesium sulfate), and the ether was removed. The crude bromo ketone mixture was dissolved in N,N-dimethylacetamide (20 ml); calcium carbonate (0.5 g) was added, and the mixture heated under reflux for 30 min. After filtration the mixture was poured into water and the product taken into ether (two 50-ml portions); the combined ether extracts were washed with water (three 50-ml portions) and dried. The ether was removed, and the mixture of unsaturated ketones thus obtained was separated by

(22) C. Djerassi, D. Marshall, and T. Nakano, *J. Am. Chem. Soc.*, **80**, 4853 (1958).

(23) See footnote *d*, Table I.
(24) E. D. Bergmann and R. Corrett, *J. Org. Chem.*, **23**, 1507 (1958).

glpc (10-ft 20% Carbowax 20M on 60–80 Chromosorb W, 150°). The products isolated in their order of elution were: (a) **4,4,5-trimethyl-Δ^2-cyclohexenone**, 62%, λ_{max}^{film} 5.95 μ [*Anal.* Calcd for $C_9H_{14}O$: C, 78.21; H, 10.21; mol wt, 138. Found: C, 7790; H, 9.93; mol wt (mass spectroscopy), 138. The nmr spectrum (CDCl$_3$ solution) showed a quadruplet centered at δ 6.25 ($J = 10$ cps) due to the two vinylic protons at C-2 and C-3]; (b) **3,4,4-trimethyl-Δ^2-cyclohexenone (XII)**, 16.5%, λ_{max}^{film} 5.95 μ [*Anal.* Calcd for $C_9H_{14}O$: mol wt, 138. Found: mol wt (mass spectroscopy), 138; n^{24}D 1.4839 (lit.[25] 1.4840)]; (c) **4,4,5-trimethyl-$^2,^5$-cyclohexadienone (XIII)**, 19.5%, λ_{max}^{film} 6.02 μ [*Anal.* Calcd for $C_9H_{12}O$: mol wt, 136. Found: mol wt (mass spectroscopy), 136].

In an analogous sequence the enamine from 2-methylpropanal and piperidine was condensed with methyl vinyl ketone to give **4-methyl-4-ethyl-Δ^2-cyclohexenone (XIV)**, 61%, a colorless oil, bp 106–109° (31 mm). *Anal.* Calcd for $C_9H_{14}O$: C, 78.21; H, 10.21; mol wt, 138. Found: C, 77.94; H, 10.27; mol wt (mass spectroscopy), 138. 1,4 Addition of methylmagnesium iodide to this cyclohexenone afforded **3,4-dimethyl-4-ethylcyclohexanone**, 73%, as a colorless oil, λ_{max}^{film} 5.78 μ. *Anal.* Calcd for $C_{10}H_{18}O$: C, 77.86; H, 11.76. Found: C, 77.71; H, 11.82. The 1,2-addition product was also obtained in this reaction, but was not characterized further. The above saturated ketone was brominated and dehydrobrominated as described above and the resulting mixture of unsaturated ketones separated by glpc (10-ft 20% Carbowax 20M on 60–80 Chromosorb W, 150°). Again three products were isolated: (a) **4,5-dimethyl-4-ethyl-Δ^2-cyclohexenone (XVI)**, 66%, λ_{max} 228 mμ [*Anal.* Calcd for $C_{10}H_{16}O$: C, 78.90; H, 10.59; mol wt, 152. Found: C, 78.97; H, 10.54; mol wt (mass spectroscopy), 152]; (b) **3,4-dimethyl-4-ethyl-Δ^2-cyclohexenone (XV)**, 21%, λ_{max}^{film} 5.95 μ, λ_{max} 238 mμ [*Anal.* Calcd for $C_{10}H_{16}O$: C, 78.90; H, 10.59; mol wt, 152. Found: C, 78.60; H, 10.36; mol wt (mass spectroscopy), 152]; (c) **4,5-dimethyl-4-ethyl-$\Delta^{2,5}$-cyclohexadienone (XVII)**, 13%, λ_{max}^{film} 6.05 μ, λ_{max} 238 mμ [*Anal.* Calcd for $C_{10}H_{14}O$: C, 79.96; H, 9.39; mol wt, 150. Found: C, 79.60; H, 9.3; mol wt (mass spectroscopy), 150].

4,4-Di-(d_3-methyl)-5-methyl-Δ^2-cyclohexenone (IIIb) (See Scheme II). The Grignard reagent from d_3-methyl iodide (3.1 ml) and magnesium (1.2 g) in ether (40 ml) was stirred under nitrogen and a solution of ethyl ethoxyacetate (3.3 g) in ether (20 ml) was added during 30 min. The reaction mixture was heated under reflux for 30 min, then left overnight at room temperature. A saturated aqueous solution of ammonium chloride was added and the ethereal layer separated. The aqueous layer was extracted with ether; the combined ether layers were dried over anhydrous magnesium sulfate, and the ether was removed. The residual oil was suspended in 15% sulfuric acid (25 ml) and stirred under nitrogen, and the mixture slowly distilled until the temperature of the distillate reached 100°. The distillate was taken up in ether (25 ml), dried over anhydrous potassium carbonate, and filtered. A further quantity of anhydrous potassium carbonate (5 g) was added, the mixture was cooled in ice, and piperidine (5 ml) added with swirling. The mixture was kept at 0° overnight, filtered, and distilled under reduced pressure. The fraction bp 97–99° (90 mm) was collected and shown by mass spectrum and glpc (5-ft 15% Apiezon on 60–80 Chromosorb W, 100°) to be 95% 1,1-di-(d_3-methyl)-2-piperidinoethene (0.76 g, 22%). The foregoing enamine (0.76 g) was cooled and stirred under nitrogen and redistilled methyl vinyl ketone (0.4 g) added. The mixture was stirred at room temperature under nitrogen for 90 hr, then 15% hydrochloric acid (6 ml) added. The mixture was left a further 24 hr, heated on a steam bath for 1 hr, diluted to 75 ml with water, and thoroughly extracted with ether. The ether extracts were washed with water and dried over anhydrous magnesium sulfate; the ether was removed and the residual oil bulb distilled under reduced pressure. **4,4-Di-(d_3-methyl)-Δ^2-cyclohexenone** was obtained as a colorless oil (0.42 g, 62%), bp 120–140° (bath) (28 mm), λ_{max}^{film} 5.95 μ. The nmr and mass spectra indicated deuterium incorporation of 98% with no rearrangement of deuterium from the two 4-d_3-methyl substituents. **4,4-Di-(d_3-methyl)-5-methyl-Δ^2-cyclohexenone (IIIb)** was prepared from the preceding ketone by the procedure used for the synthesis of the unlabeled analog III described earlier. The nmr spectrum showed a quadruplet at δ 6.25 ($J = 10$ cps) (two vinylic protons) and a doublet at δ 0.95 ($J = 6$ cps) (three methyl protons). The nmr and mass spectra indicated that deuterium incorporation was 98% with no rearrangement of deuterium from the two 4-d_3-methyl substituents.

4-Methyl-4-phenyl-Δ^2-cyclohexenone (XVIII). A solution of α-phenylpropionaldehyde (25.0 g) and redistilled methyl vinyl ketone (15.0 g) in *t*-butyl alcohol (125 ml) was stirred under nitrogen and cooled in ice during the dropwise addition of 30% aqueous Triton B hydroxide (31 ml). The addition required 15 min and the mixture was stirred at 0° a further 2 hr. The reaction mixture was poured into water and extracted thoroughly with ether. The ether extract was washed with water and dried over anhydrous magnesium sulfate and the ether removed. The crude residue was distilled at reduced pressure to give **4-methyl-4-phenyl-Δ^2-cyclohexenone** as a colorless oil which crystallized on scratching, bp 110–120° (0.5 mm). On recrystallization from ether at low temperature the ketone afforded colorless needles, mp 40°. *Anal.* Calcd for $C_{13}H_{14}O$: mol wt, 186. Found: mol wt (mass spectroscopy), 186.

4,5-Dimethyl-4-phenyl-Δ^2-cyclohexenone (XIX). A stirred solution of α-phenylpropionaldehyde (1.34 g) and pent-2-en-3-one[26] (0.84 g) in *t*-butyl alcohol (5 ml) was cooled to 5° in ice and 30% aqueous Triton B hydroxide (1.5 ml) was added during 30 min. The mixture was stirred at 5–10° a further 2 hr and poured into water, and the product was extracted into ether. The ether extract was washed with water and dried and the ether removed. The residue was bulb distilled at bath temperature, 145–150° (0.5 mm), to give **4,5-dimethyl-4-phenyl-Δ^2-cyclohexenone** as a pale yellow viscous oil which did not crystallize at room temperature. A portion was purified by glpc (5-ft 20% silicone rubber on 60–80 Chromosorb W, 175°). *Anal.* Calcd for $C_{14}H_{16}O$: C, 83.96; H, 8.05; mol wt, 200. Found: C, 83.75; H, 8.01; mol wt (mass spectroscopy), 200.

4,5-Dimethyl-4-(p-bromophenyl)-Δ^2-cyclohexenone (XX). A mixture of p-bromoacetophenone (10 g), ethyl chloroacetate (6.75 g), and *t*-butyl alcohol (50 ml) was stirred under nitrogen and cooled to 15°. A solution of potassium *t*-butoxide (6.15 g) in *t*-butyl alcohol (50 ml) was added during 1.5 hr. A gelatinous precipitate formed and made stirring difficult. The mixture was left at 21° for 2 days, poured into water (200 ml), and extracted with ether (two 100-ml portions). The ether extract was washed with water and dried over anhydrous magnesium sulfate and the ether removed. The residue was distilled (3 mm) and the fraction bp 140–155° collected and redistilled (1 mm). The glycidic ester (5.6 g) was obtained as an oil, bp 125–140°, and was used directly in the next step. The crude ester (5.3 g) was dissolved in dry ethanol (10 ml) and sodium methoxide (1 g) was added. Upon addition of water (0.34 ml), the sodium salt of the glycidic acid began to precipitate, and was collected after 24 hr, washed with ether, and air dried. The salt was suspended in ether (50 ml), and dry hydrogen chloride was bubbled through the mixture for 30 min. Heat was evolved; the salt dissolved, and finely divided sodium chloride separated. The mixture was filtered on Kieselguhr; the residue was washed with ether and the combined ethereal solutions were evaporated, leaving a yellow gum which crystallized on trituration with pentane. A solution of sodium bicarbonate (4 g) in water (20 ml) was added and the mixture allowed to stand for 2 hr, then heated on a steam bath for 15 min. The cooled mixture was extracted with ether, and the ether extract washed with water, dried over anhydrous magnesium sulfate, and evaporated. The residual oil was distilled under reduced pressure to give α-(p-bromophenyl)propionaldehyde as a pale yellow oil (1.72 g), bp 158–163° (36 mm). *Anal.* Calcd for C_9H_9BrO: C, 50.73; H, 4.26. Found: C, 50.54; H, 4.01. **4,5-Dimethyl-4-(p-bromophenyl)-Δ^2-cyclohexenone** was prepared from aldehyde (1 g) and pent-2-en-3-one (0.4 g) in a manner analogous to that described above for the preparation of 4,5-dimethyl-4-phenyl-Δ^2-cyclohexenone. It was obtained as colorless needles, mp 118°. *Anal.* Calcd for $C_{14}H_{15}BrO$: C, 60.23; H, 5.42. Found: C, 60.36; H, 5.73.

3-Methyl-4,4-diphenyl-Δ^2-cyclohexenone (XXII). This ketone was prepared from 4,4-diphenyl-Δ^2-cyclohexenone[27] by 1,4 addition of methylmagnesium iodide, followed by bromination and dehydrobromination of the resulting saturated ketone using procedures already described in the synthesis of 4,4,5-trimethyl-Δ^2-cyclohexenone (III). The 1,4-addition product in the first step was separated from some 1,2-addition product (allylic alcohol) by fractional crystallization from methanol. Separation of the mixture of unsaturated ketones obtained in the final step was achieved by repeated thin layer chromatography on silica gel GF$_{254}$ (Stahl)

(25) E. R. Buchman and H. Sargent, *J. Org. Chem.*, 7, 140 (1942).

(26) S.-O. Lawesson, E. H. Larsen, G. Sundstrom, and H. J. Jakobsen, *Acta Chem. Scand.*, 17, 2216 (1963).

(27) See footnote *h*, Table I.

containing 5% silver nitrate, using 20% ether in benzene as eluent. Bands were detected by ultraviolet light, separated, and extracted with ether. Only two products were isolated, and both were shown by infrared spectroscopy to be unsaturated ketones. The more easily eluted product was not obtained free from saturated ketone even on repeated chromatography. The less mobile product crystallized from methanol–water as colorless prismatic needles, mp 106°. The nmr spectrum showed a singlet at δ 6.2 integrating for one proton (vinylic) and a doublet at δ 1.61 (J = 1 cps) integrating for three protons (methyl group attached to double bond), indicating that the compound was **3-methyl-4,4-diphenyl-Δ^2-cyclohexenone (XXII)**. *Anal.* Calcd for $C_{19}H_{18}O$: C, 86.99;

H, 6.92; mol wt, 262. Found: C, 86.57; H, 6.86; mol wt (mass spectroscopy), 262.

4,5-Dimethyl-Δ^2-cyclohexenone (XXIII). 3,4-Dimethylcyclohexanol was oxidized by Jones' reagent[10] to 3,4-dimethylcyclohexanone. Bromination and dehydrobromination as already described gave a mixture of unsaturated ketones, which was separated by glpc (10-ft 20% IGEPAL on 60–80 Chromosorb W, 150°). The most abundant product was shown by infrared (λ_{max}^{film} 5.95 μ) and ultraviolet (λ_{max} 228 mμ) spectra to be 4,5-dimethyl-Δ^2-cyclohexenone. *Anal.* Calcd for $C_8H_{12}O$: C, 77.37; H, 9.74; mol wt, 124. Found: C, 77.24; H, 9.57; mol wt (mass spectroscopy), 124. The other isomer was not characterized further.

Mass Spectrometry in Structural and Stereochemical Problems. CXXXIV.[1] Electron Impact Induced Alkyl and Aryl Rearrangements in α-Arylidene Cyclic Ketones[2]

R. L. N. Harris,[3a] F. Komitsky, Jr.,[3b] and Carl Djerassi

Contribution from the Department of Chemistry, Stanford University, Stanford, California 94305. Received April 4, 1967

Abstract: The mass spectra of a number of alkyl- and aryl-substituted α-arylidene cyclic ketones have been measured and the mechanism and scope of an electron impact induced alkyl (aryl) rearrangement occurring in these compounds is examined. Other fragmentation processes occurring in this class of compounds are also discussed.

Ketones of type I display a prominent peak in their mass spectra at *m/e* 69 which has been shown[4] to be due to the formation of the ion a, arising from a 1,2 rearrangement of the angular methyl group from C-10 to C-4 prior to fragmentation. In an earlier paper[5] the mechanism and scope of this rearrangement was discussed and it was found to occur in ketones of general formula II where R_1 = H, Me, Et, and Ph, and R_2 and R_3 are either methyl groups or part of a second alicyclic ring (five, six, or seven membered) Of particular interest was the fact that certain closely related ketones (II, R_3 = H) did not display any significant

Scheme I
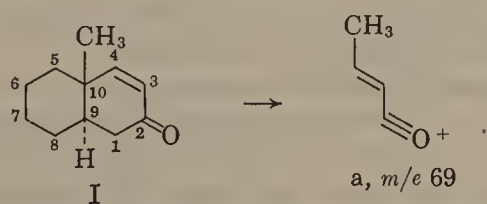
rearrangement ions in their mass spectra. From this and other evidence it was concluded that the C-5 alkyl substituent was implicated in the rearrangement process; of the various plausible mechanistic rationalizations outlined earlier[5] only that summarized in Scheme I is compatible with all of the experimental results.

An earlier communication[6] has drawn attention to the occurrence of a related rearrangement in the mass spectra of 2-arylidene-1-decalones. Thus, the base peak in the mass spectrum of *trans*-2-furfurylidene-9-methyl-1-decalone (III) and the analogous steroidal D-homo ketone IV occurs at *m/e* 121 and was shown by exact mass measurements to correspond to C_8H_9O. This peak was shifted to *m/e* 124 in the spectrum of the 9-d_3-methylated analog IIIa and to *m/e* 122 in that of the 3-d_1 analog IIIb, whereas in the spectrum of the compound lacking the angular methyl group (V) the base

III, R_1 = Me, R_2 = H
IIIa, R_1 = CD$_3$, R_2 = H
IIIb, R_1 = Me, P$_2$ = D
V, R_1 = H, R. H

IV

(1) For paper CXXXIII see P. Brown and C. Djerassi, *Angew. Chem.*, in press.

(2) Financial assistance by the National Institutes of Health (Grants No. AM-04257 and CA-07195) is gratefully acknowledged. The purchase of the Atlas mass spectrometer was made possible through NASA Grant NsG 81-60.

(3) Postdoctoral Research Fellow: (a) 1965–1966; (b) 1964–1965.

(4) F. Komitsky, Jr., J. E. Gurst, and C. Djerassi, *J. Am. Chem. Soc.*, 87, 1398 (1965).

(5) R. L. N. Harris, F. Komitsky, Jr. and C. Djerassi, *ibid.*, 89, 4765 (1967).

(6) C. Djerassi, A. M. Duffield, F. Komitsky, Jr., and L. Tökes, *ibid.*, 88, 860 (1966).

peak occurred at m/e 107. Appropriate mass shifts were encountered in the benzylidene (m/e 131), p-chlorobenzylidene (m/e 165–167), and p-methylbenzylidene (m/e 145) analogs of III. In those examples where both cis- and trans-ring-fused isomers were isolated, there were no significant differences in their mass spectra.

From these results it was concluded[6] that the intense m/e 121 peak in the spectrum of III was due to ion b, which contains the furfurylidene moiety, together with the adjacent carbon atoms 2 and 3 and the bridgehead C-9 methyl substituent. This ion must have arisen by a rearrangement process in which the angular methyl group migrates from its position at the ring junction to C-2 prior to fragmentation. Two possible mechanistic alternatives were proposed to account for this rearrangement, and they are set out in Scheme II. Both mechanisms involve at first the loss of carbon monoxide to give the ionized 1-furfurylidene-8-methylhydrindan (c), which may fragment by either of two pathways (i and ii) to give the charged species b.

Scheme II

c

b, m/e 121
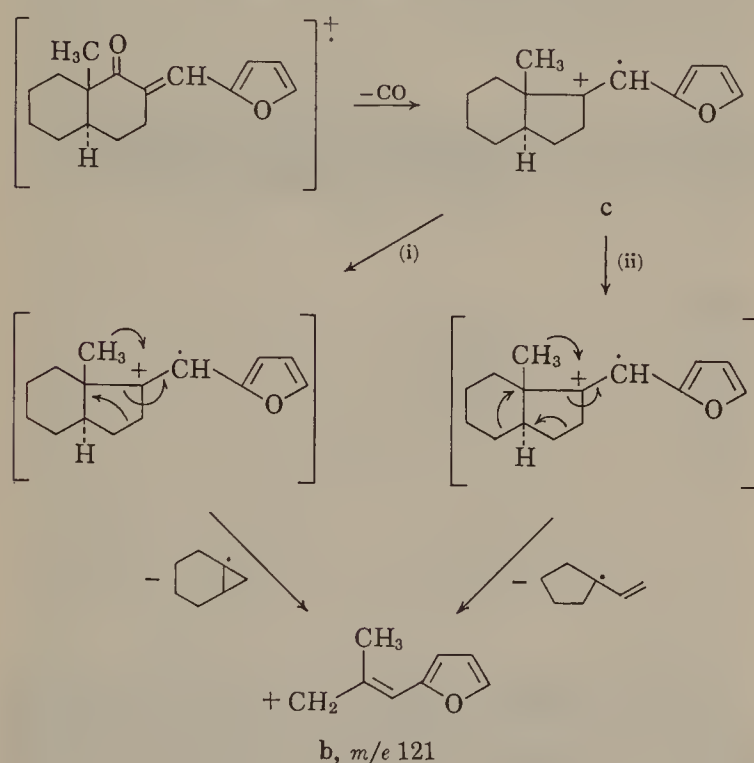
In support of the first step (carbon monoxide ejection), common to both rearrangement sequences, it was shown that the mass spectrum of the benzylidenehydrindan VI (analogous to the intermediate (M − CO) species c, Scheme II) also exhibited an intense rearrangement ion at m/e 131, corresponding to b (furfuryl replaced by phenyl). It should be noted that

VI
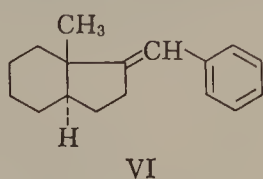
the two alternatives (i and ii) in Scheme II proposed to account for the methyl migration and concomitant bond fissions are directly analogous to those considered for the related electron impact induced methyl migration in α,β-unsaturated cyclic ketones.[4,5] As in the unsaturated ketone series the two pathways may be distinguished by a consideration of the scope of the rear-

rangement; for example, if the rearrangement follows path i then ketones such as VII which have no substituent at C-5 (corresponding to the site of ring juncture in the decalone III) should still show the rearrangement peak (m/e 121). However, if the rearrangement follows path ii, then C-5 alkylated cyclohexanones such as VIII should display the rearrangement peak, while VII should not.

VII   VIII
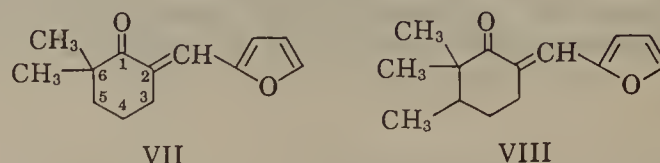
Accordingly the 2-furfurylidene-6,6-dimethyl- and 5,6,6-trimethylcyclohexanones (VII and VIII, respectively) were prepared and their mass spectra measured. The present paper considers the mechanistic implications of these results and further delineates the scope of the rearrangement by a consideration of the mass spectra of α-arylidene cyclic ketones in which the migrating group is methyl, ethyl, or phenyl and the aryl group is furfuryl, phenyl, or substituted phenyl (see Table I). The influence of ring size and the effect of the stereochemistry of the ring juncture in bicyclic ketones on the rearrangement process are also considered. The involvement of the M − CO species in the rearrangement process (see Scheme II) has been inferred by measuring the mass spectra of two related benzylidenehydrindans and a benzylidenecyclopentane.

Synthetic Studies

2-Arylidene-9-alkyl-1-decalones were prepared by base-catalyzed condensation of the appropriate aldehyde with 1-decalone[7] followed by alkylation at C-9. In some instances the mixture of cis and trans isomers was separated by fractional crystallization; in others the mixture was used directly for mass spectral examination. The same general approach was utilized in the synthesis of the 2-arylidene-6,6-dialkylcyclohexanones.

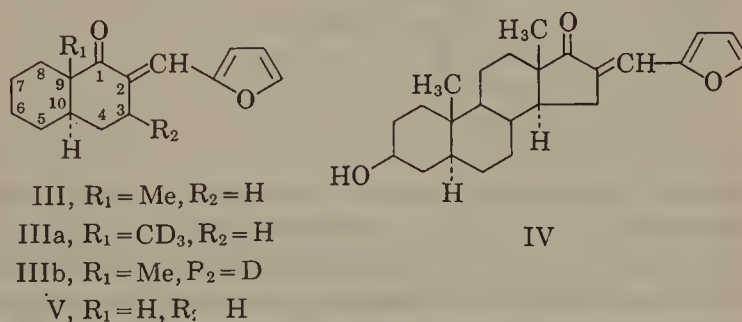2-Furfurylidene-5,6,6-trialkylcyclohexanones (VIII) were obtained by condensation of 2,3-dimethylcyclohexanone (prepared from the corresponding phenol[8]) with furfural followed by alkylation.

A somewhat more circuitous route had to be employed for 2-furfurylidene-5,6-dimethyl-6-phenylcyclohexanone (XXII). 4,5-Dimethyl-4-phenyl-Δ^2-cyclohexenone[5] was converted to the 2,3-epoxide which was reduced with hydrazine[9] to a mixture of epimeric 5,6-dimethyl-6-phenyl-Δ^2-cyclohexenols. Jones oxidation[10] of the mixture gave 5,6-dimethyl-6-phenyl-Δ^2-cyclohexenone which was hydrogenated (at atmospheric pressure over 10% palladium on carbon catalyst in ethyl acetate) and condensed as before with furfuraldehyde to give the required 2-furfurylidene derivative.

cis-1-Benzylidene-8-methylhydrindan (VI) was obtained from cis-8-methyl-1-hydrindanone,[11] which was treated with excess benzylmagnesium chloride in ether

(7) W. S. Johnson, B. Bannister, and R. Pappo, J. Am. Chem. Soc., 78, 6336 (1956).
(8) (a) H. E. Ulery and J. H. Richards, ibid., 86, 3113 (1964); (b) W. Hückel and M. G. E. Ibrahim, Ber., 91, 1970 (1958).
(9) M. P. Cava and B. R. Vogt, J. Org. Chem. 30, 3775 (1965).
(10) K. Bowden, I. M. Heilbron, E. R. H. Jones, and B. C. Weedon, J. Chem. Soc., 39 (1946).
(11) W. S. Johnson, J. Am. Chem. Soc., 66, 215 (1944).

and the resulting alcohol dehydrated with phosphorus oxychloride in pyridine. A mixture of the exocyclic (VI) and endocyclic (*cis*-1-benzyl-8-methylhydrindene) products was isolated, but its separation was readily effected by vapor phase chromatography. The synthesis of the related model compound, 1-benzylidene-2,2,3-trimethylcyclopentane (XXIII), utilized as starting material 2,2,3-trimethylcyclopentanone, which was prepared from the corresponding cyclohexanone furfurylidene derivative following the procedure[11] used in the preparation of 8-methylhydrindanone from 9-methyl-2-furfurylidene-1-decalone. Reaction of the cyclopentanone with benzylmagnesium chloride followed by dehydration gave a mixture of benzylidenecyclopentane and benzylcyclopentene which was separable by vapor phase chromatography.

The deuterium-labeled compounds were generally prepared by the same methods used for the unlabeled analogs. Thus α'-methyl-d_3-α-arylidene ketones were synthesized by alkylation of the appropriate arylidene ketone with methyl-d_3 iodide. α'-Deuterated α-arylidene ketones were prepared by exchanging the α' hydrogen in methanol-d_1 and heavy water in the presence of base.

The synthesis of *trans*-2-furfurylidene-9-methyl-1-decalone-3-d_1 (IIIb) is outlined in Scheme III. *trans*-9-Methyl-3-oxo-1-methoxy-$\Delta^{1,6}$-hexahydronaphthalene[12] was reduced with lithium aluminum deuteride and the product treated with sulfuric acid to give *trans*-9-methyl-1-keto-$\Delta^{2,6}$-hexahydronaphthalene-3-d_1. The unsaturated ketone was reduced at room temperature over palladium-on-carbon catalyst to *trans*-9-methyl-1-decalone-3-d_1 which was condensed with furfural to yield the required 2-furfurylidene derivative IIIb. The corresponding benzylidene derivative was prepared in the same manner using benzaldehyde instead of furfural in the final step.

Scheme III
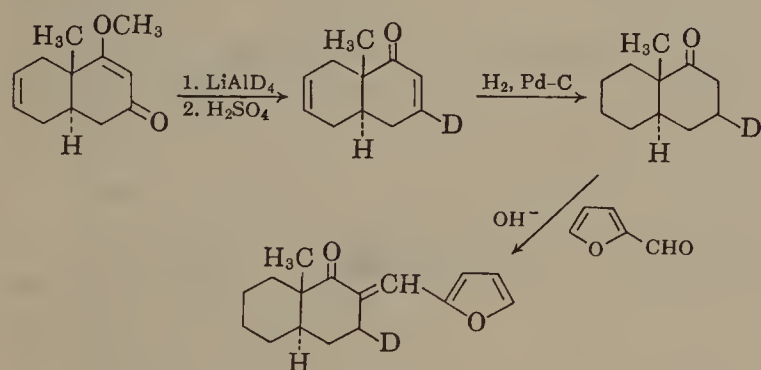
Discussion of the Mass Spectra

The Rearrangement Ion. The results listed in Table I show that the rearrangement ion (of type b) is a prominent feature in the mass spectra of many α-arylidene-α'-methyl cyclic ketones, in many instances being the base peak of the spectrum. The intensity of this ion is recorded both as per cent total ionization ($\% \Sigma_{40}^{M^+}$) and as per cent abundance relative to the most intense peak ($\%$ RA); the same data are also presented for both the molecular ion (M⁺) and the M − CO ion where applicable. As noted in Table I, many of the spectra were measured at both 70 and 12 ev. High-resolution mass spectrometry was employed to confirm

(12) C. Djerassi, E. Lund, and A. A. Akhrem, *J. Am. Chem. Soc.*, **84**, 1249 (1962).

in every instance the molecular composition of the appropriate ions. Further evidence for the structure of the rearrangement ion is given by the deuteration studies (see last column in Table I), which show conclusively that both the angular methyl substituent (at C-9 in the decalones and C-6 in the cyclohexanones) and the C-3 carbon atom are incorporated in the rearrangement species. Appropriate mass shifts for this ion in the mass spectra of other arylidenedecalones (X–XIII) demonstrate that in every case the arylidene moiety forms part of the rearrangement ion. Structure b for this ion is in complete accord with these observations.

Several examples are also presented in which the migrating group is ethyl (XVII, XVIII, XXI), hydrogen (V, XIV–XVI), and phenyl (XXII). Again, deuteration studies support the structures assigned to the rearrangement ion in all except the last of these examples.

The two mechanistic paths proposed[6] for the formation of ion b have in common the loss of carbon monoxide in the first step (see Scheme II), giving rise to an intermediate which may be formulated as an ionized furfurylidenehydrindan (c). The mass spectra of the benzylidenehydrindan VI and its 8-methyl-d_3 analog VIa display intense peaks at m/e 131 and 134, respectively, indicating that these compounds also give rise to the ion involving rearrangement of the angular methyl group. This alone is insufficient evidence to prove the intermediacy of the arylidenehydrindan in the rearrangement process. However, consideration of the low-voltage spectra (Table I) reveals that, whereas the intensity of the M − CO peak increases markedly at lower ionizing potential, the intensity of the rearrangement ion in most cases decreases. This indicates that the loss of carbon monoxide is an energetically favorable primary fragmentation process, whereas the alkyl migration is less favorable and almost certainly represents a secondary process. There is strong evidence, therefore, that the M − CO species is in fact an intermediate in the rearrangement, as previously suggested (see Scheme II). The benzylidenecyclopentane derivative XXIII also displays a prominent rearrangement ion (m/e 131) in its mass spectrum, thus offering support in the monocyclic series for the intermediacy of an M − CO species in the rearrangement step.

Two pathways have been proposed for rearrangement and fragmentation of the M − CO species to give the rearrangement ion (see Scheme II), the distinguishing feature being the involvement of the C-5 alkyl substituent in one of them (path ii). Examination of the results in Table I shows that the abundance of the rearrangement ion in the ketone VII is very small, whereas in VIII, which differs from VII only in possessing a methyl substituent at C-5, the rearrangement ion is *eleven times* more abundant. Similarly the dimethyl benzylidene ketone XX shows very little rearrangement, whereas the C-5 substituted ketones XXI and XXII both show significant rearrangement ions. These results strongly suggest that the C-5 alkyl substituent is involved in the rearrangement process, a striking parallel to the conclusions reached about the course of alkyl rearrangement in α,β-unsaturated cyclic ketones.[5]

A careful scrutiny of the relevant mass spectra has revealed in every example the appropriate meta-

Table I. Electron Impact Induced Alkyl and Aryl Migrations in Cyclic α-Arylidene Ketones
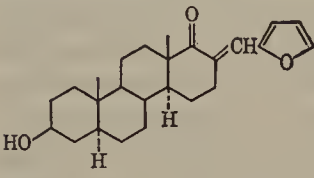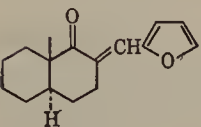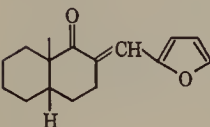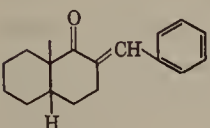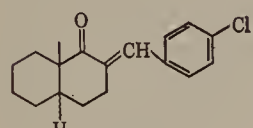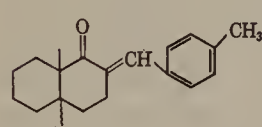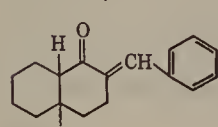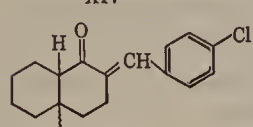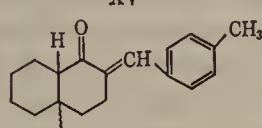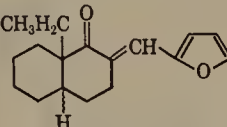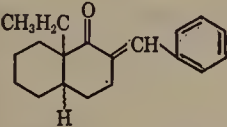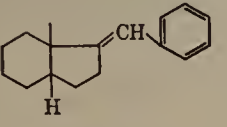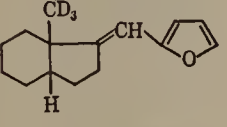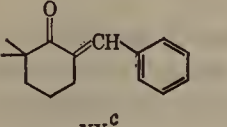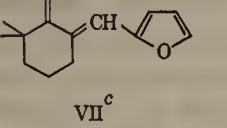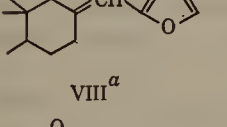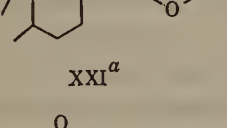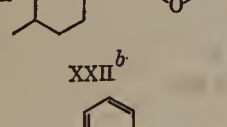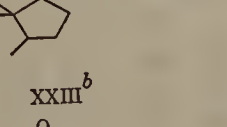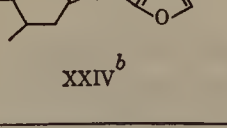
Compd	M+, 70 ev %Σ_{40}M+	M+, 70 ev %RA	M+, 12 ev %Σ_{40}M+	M+, 12 ev %RA	—M—CO,— 70 ev %Σ_{40}M+	—M—CO,— 70 ev %RA	—M—CO,— 12 ev %Σ_{40}M+	—M—CO,— 12 ev %RA	m/e	Rearrangement ion, 70 ev %Σ_{40}M+	Rearrangement ion, 70 ev %RA	Rearrangement ion, 12 ev %Σ_{40}M+	Rearrangement ion, 12 ev %RA	Deuterated analogs
IV [c,f]	1.5	20			2.0	27			121	7.4	100			18-Methyl-d_3 (IVa), m/e 121 → 124
III [c,f]	3.3	46			2.9	41			121	7.1	100			9-Methyl-d_3 (IIIa), m/e 121 → 124; 3-d_1 (IIIb), m/e 121 → 122
IX [c,f]	2.9	34			3.9	45			121	8.6	100			
X [a,f]	4.7	57	17.6	59	8.2	100	29.8	100	131	4.0	48	3.0	10	9- Methyl-d_3 (Xa), m/e 131 → 134
XI [a,f]	4.7	57	11.0	82	6.2	68	13.4	100	131	3.2	35	4.3	32	3-d_1 (XIa), m/e 131 → 132
XII [a]	1.3	22	8.6	29	7.5	133[d]	38	133[d]	165[d] 167	4.1	73	3.4	12	
XIII [a]	4.0	77	20.9	100	5.1	100	18.9	90	145	4.5	88	4.2	20	
V [c,f]	4.5	33			2.2	16			107	13.6	100			
XIV [c,f]	4.8	53			1.2	13			117	9.2	100			9-d_1 (XIVa), m/e 117 → 118
XV [c]	1.9	32			1.5	26			151[d] 153	6.3	109			
XVI [c]	2.1	20	20	100	0.8	8	17.9	90	131	10.4	100	4	20	

Table I (*Continued*)

Compd	M+, 70 ev % Σ_{40}M+	% RA	M+, 12 ev % Σ_{40}M+	% RA	—M−CO,— 70 ev % Σ_{40}M+	% RA	—M−CO,— 12 ev % Σ_{40}M+	% RA	m/e	Rearrangement ion, 70 ev % Σ_{40}M+	% RA	Rearrangement ion, 12 ev % Σ_{40}M+	% RA	Deuterated analogs
XVII[c]	4.9	61			0.13	1.6[e]			135	1.0	13			
XVIII[c]	0.9	11			0.2	2.5[e]			145	0.6	7			
VI[c]	4.1	35							131	6.3	53			8-Methyl-d_3 (VIa), m/e 131 → 134
XIX[b]	9.6	31			2.2	7			124	0.3	1			
XX[c]	3.7	38			4.0	42[g]			131	0.7	7			
VII[c]	3.6	32			4.2	37			121	1.0	9			
VIII[a]	4.7	43	56	100	4.1	37	23.6	42	121	11.0	100	1.1	2	6-Methyl-d_3 (VIIIa), m/e 121 ↗124 ↘121
XXI[a]	3.1	25			1.9	15.4[e]			121	1.7	14			2-β-Ethyl-d_3 (XXIa),[c] m/e 135 → 138
									135	0.5	4			
XXII[b]	8.0	59			13.5	100			121	5.0	37			
									183	2.0	15			
XXIII[b]	3.7	35	53.8	100					131	9.3	74	3.8	7	
XXIV[b]	8.8	25			2.1	6			121	0.7	2			

a Mass spectrum recorded on an AEI MS-9 mass spectrometer. *b* Mass spectrum recorded on an Atlas CH-4 spectrometer. *c* Mass spectrum recorded on a CEC Model 21–103C mass spectrometer. *d* This value includes contributions from both ions containing the two isotopes of chlorine. *e* Calculated as the M − CO peak by subtracting the proportion of M − C_2H_4 as determined by high-resolution mass spectrometry. *f* The authors wish to thank Professor W. S. Johnson of this department for a generous gift of this compound. *g* High-resolution mass measurements showed that no M − C_2H_4 ion was produced.

Harris, Komitsky, Djerassi | Rearrangements in α-Arylidene Cyclic Ketones

Scheme IV. Major Fragmentation Pathways of *trans*-2-Furfurylidene-9-methyl-1-decalone (III) after Electron Impact

Figure 1. Mass spectrum of *trans*-2-furfurylidene-9-methyl-1-decalone (III); see Scheme IV.

stable ion for the loss of carbon monoxide from the molecular ion, a result to be expected in view of the ease of this fragmentation process. However, the generation of the rearrangement ion b from the M — CO precursor was supported in only one instance by the appearance of a metastable ion—in the mass spectrum of 2-furfurylidene-5,6,6-trimethylcyclohexanone (VIII).

In conclusion it may be stated that the electron impact induced migration of an alkyl group in α-arylidene-cyclohexanones and -decalones takes place after loss of carbon monoxide from the molecular ion in what is most probably a concerted process involving participation of another alkyl substituent at C-5 in the cyclohexanones (C-10 in the corresponding decalones), as indicated by path ii, Scheme II.

Other Fragmentation Processes

Since nothing has so far been published on the electron impact induced fragmentation of arylidene ketones and related compounds, we summarize below some of their typical decomposition modes.

trans-2-Furfurylidene-9-methyl-1-decalone (III). The mass spectrum is shown in Figure 1, and the major

fragmentation pathways (asterisks denote presence of the appropriate metastable peak) are set out in Scheme IV; supporting evidence from deuteration studies is summarized in Table II. It should be recognized that the structures given in this and the subsequent schemes are used for illustrative purposes only to describe the over-all course of the fragmentations and may bear little relation to the actual structures of the ions. As can be seen from Scheme IV there are several major fragmentation pathways: loss of a methyl radical and/or carbon monoxide leads to fragments a, c, and d, while subsequent bond fissions in d afford b, e, and f. Hydrogen transfer (provisionally postulated from C-10) followed by cleavage and subsequent loss of carbon monoxide leads to ions g, h, and i, thus accounting for most of the abundant peaks in the upper mass range of Figure 1. The mass spectrum of the *cis* isomer IX is almost identical. Analogous fragmentations also occur in the arylidene series (X–XIII).

Table II. Summary of Major Fragment Ions of *trans*-2-Furfurylidene-9-methyl-1-decalone (III) and Deuterated Derivatives

Compd	M+	a	b	c	d	e	f	g	h	i
III	244	229	121	201	216	106	105	109	135	107
IIIa	247	229	124	201	219	106	105	112	135	107
IIIb	245	230	122	202	217	107	106	109	136	108

cis-1-Benzylidene-8-methylhydrindan (VI) (Figure 2). The main fragmentation pathways are summarized in Scheme V, with supporting evidence from deuteration studies set out in Table III. Again, the rearrangement ion b is a prominent feature of the mass spectrum, but now the base peak d (m/e 91) is the tropylium cation, arising from a hydrogen migration and subsequent

Figure 2. Mass spectrum of *cis*-1-benzylidene-8-methylhydrindan (VI); see Scheme V.

Figure 3. Mass spectrum of 2-furfurylidene-5,6,6-trimethylcyclohexanone (VIII); see Scheme VI.

Table III. Summary of Major Fragment Ions of *cis*-1-Benzylidene-8-methylhydrindan (VI) and Its 8-Methyl-d_3 Derivative (VIa)

			m/e values for fragment ions		
Compd	M⁺	a	b	c	d
VI	226	211	131	135	91
VIa	229	211	134	135	91

benzylic cleavage as depicted in Scheme V. There is some charge retention on the alicyclic part of the molecule after this cleavage, giving rise to the ion of mass 135, probably best represented as the allyllically stabilized tertiary carbonium ion c. It is of interest that the isomeric *cis*-1-benzyl-8-methyl-Δ^1-hydrindene (VI′), which was obtained as a by-product in the synthe-

sis of VI, has a very similar mass spectrum with prominent peaks at m/e 91 (base peak), 135, and 211, but no significant peak at m/e 131.

2-Furfurylidene-5,6,6-trimethylcyclohexanone (VIII) (Figure 3). The principal modes of fragmentation (Scheme VI) show a striking parallel to those of the furfurylidene decalone (III, Scheme IV). Again, the principal ions are generated by three main pathways: the alkyl rearrangement leading to the base peak b at m/e 121, loss of carbon monoxide and/or a methyl radical giving ions a, c, d, and subsequently e and f, and the hydgroen rearrangement and cleavage giving rise to ions g, h, and i. Similar mass spectra are shown by the analogous 2-furfurylidene-5,6-dimethyl-6-ethylcyclohexanone (XXI) and 2-furfurylidene-5,6-dimethyl-6-phenylcyclohexanone (XXII). An important difference in the former is the occurrence of a McLafferty rearrangement now possible because of the 6-ethyl substituent. This gives rise to an M − C_2H_4 peak distinguishable from the M − CO peak by high-resolution mass spectrometry and by deuterium labeling of the terminal methyl group in the 6-ethyl substituent (XXIa).

Scheme V. Major Fragmentation Pathways of *cis*-1-Benzylidene-8-methylhydrindan (VI) after Electron Impact

Table IV. Summary of Major Fragment Ions of 2-Furfurylidene-5,6,6-trimethylcyclohexanone (VIII) and Its 6-Methyl-d_3 Derivative (VIIIa)

					m/e values for fragment ions				
Compd	M⁺	a	b	c	d	e	f	g	h	i
VIII	218	203	121	190	175	106	105	83	135	107
VIIIa	221	203	121	193	175	106	105	86	135	107
		206	124		178					

2-Furfurylidene-6,6-dimethylcyclohexanone (VII). The mass spectrum (Figure 4) differs from that (Figure 3) of the trimethyl analog VIII in that the peak at m/e 121 is greatly diminished. All other features of the two spectra are quite similar.

1-Benzylidene-2,2,3-trimethylcyclopentane (XXIII). The mass spectrum (Figure 5) resembles closely that (Figure 2) of the related benzylidenehydrindan VI. Again there is a pronounced M − 15 peak, alkyl rear-

Scheme VI. Major Fragmentation Pathways of 2-Furfurylidene-5,6,6-trimethylcyclohexanone (VIII) after Electron Impact

m/e 218

a, *m/e* 203

c, *m/e* 190

d, *m/e* 175

g, *m/e* 83

h, *m/e* 135

e, *m/e* 106

b, *m/e* 121

C_7H_7O
i, *m/e* 107

C_7H_5O
f, *m/e* 105
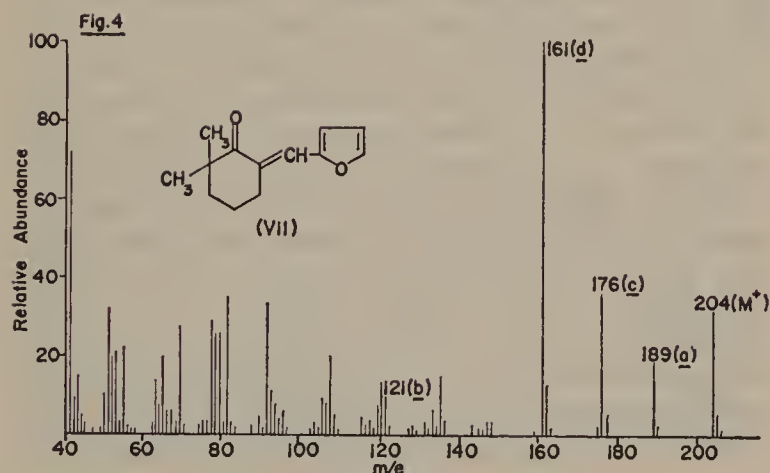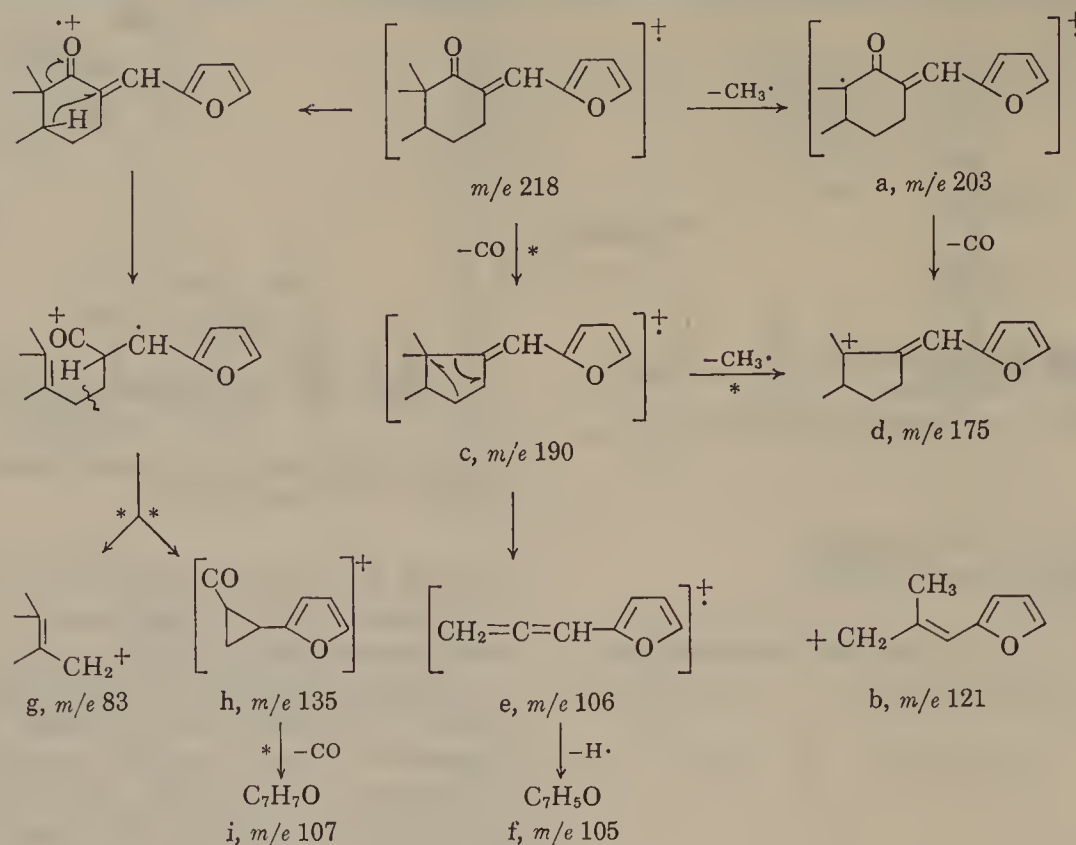
Figure 4. Mass spectrum of 2-furfurylidene-6,6-dimethylcyclohexanone (VII); the ions of mass 189, 176, and 161 are the appropriate analogs of ions a, c, and d in Scheme VI, while ion b (*m/e* 121) is identical with that depicted in Scheme VI.

Figure 5. Mass spectrum of 1-benzylidene-2,2,3-trimethylcyclopentane (XXIII); ions b and d are identical with those shown in Scheme V, while the ions of mass 185 and 109 are the appropriate analogs of ions a and c in that scheme.

rangement leads to an intense peak at *m/e* 131, and hydrogen rearrangement followed by cleavage gives the tropylium cation (*m/e* 91) and the cyclopentene cation

Figure 6. Mass spectrum of 2-furfurylidene-4,5,5-trimethylcyclopentanone (XXIV); see Scheme VII.

(*m/e* 109). The latter corresponds to the hydrindene cation c (*m/e* 135) in Scheme V. At 12 ev the only significant fragmentation is loss of a methyl radical.

2-Furfurylidene-4,5,5-trimethylcyclopentanone (XXIV). The mass spectrum (Figure 6) is much simpler than that (Figure 3) of the corresponding cyclohexanone (VIII). It is immediately apparent that the alkyl rearrangement (*m/e* 121) is essentially absent in a five-membered ketone, and this was confirmed by examining the mass spectra of some 16-furfurylidene-17-keto steroids. The principal modes of fragmentation are summarized in Scheme VII. Again loss of carbon monoxide and/or a methyl radical occurs, giving rise to ions a, b, and c. The dominant feature of the spectrum, however, is an intense peak at *m/e* 106. High-resolution mass spectrometry shows that this ion has the composition C_7H_6O, and metastable peaks support its proposed genesis by elimination of trimethylethylene to give d (*m/e* 134) and subsequent loss of carbon monoxide to e. The fragmentation of the furfurylidenehydrindanone analog XIX is completely analogous and requires no further discussion.

Scheme VII. Major Fragmentation Pathways of 2-Furfurylidene-4,5,5-trimethylcyclopentanone (XXIV) on Electron Impact

m/e 204

b, m/e 176

$* \downarrow -C_5H_{10}$

$C_8H_6O_2$
d, m/e 134

$\downarrow -CH_3\cdot$

$\downarrow -CH_3\cdot$

a, m/e 109

c, m/e 161

$* \downarrow -CO$

C_7H_6O
e, m/e 106
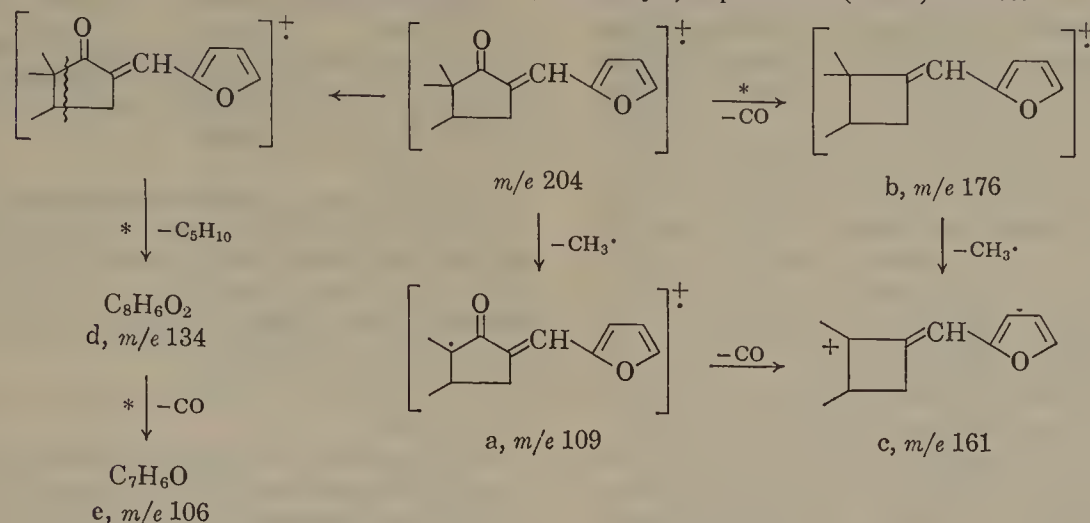
Experimental Section[13]

2-Arylidene-1-decalones and 9-Alkyl Derivatives. These compounds (Table I, XII–XVIII) were prepared by condensation of 1-decalone with the appropriate aldehyde and subsequent alkylation with the appropriate alkyl halide.[7] The products were characterized by their mass spectra which showed the appropriate molecular ion in each case.

trans-2-Furfurylidene-9-methyl-d_3-1-decalone (IIIa). *trans*-9-Methyl-d_3-1-decalone[14] (4.5 mg) in 96% ethanol (0.04 ml) was treated with 15% aqueous caustic soda (0.01 ml) and freshly distilled furfuraldehyde (0.005 ml) was added. The reaction mixture was left at room temperature under a nitrogen atmosphere for 6 hr, and the crystalline product was collected. Recrystallization from methanol gave the *furfurylidene derivative* as cream prisms, mp 108–109°.

2-Furfurylidene-5,6,6-trialkylcyclohexanones. 2,3-Dimethylcyclohexanone[8] (2 g) and redistilled furfuraldehyde (1.6 g) were stirred in an atmosphere of nitrogen during the addition of sodium methoxide (0.9 g) in methanol (15 ml). The addition was carried out during 5 min and the temperature was kept below 50°. The mixture was left overnight and poured into water (250 ml), and the solid product was collected and recrystallized from hexane, giving **2-furfurylidene-5,6-dimethylcyclohexanone** as yellow prismatic needles, mp 54.5–55.5°.

Anal. Calcd for $C_{13}H_{16}O_2$: C, 76.44, H, 7.90. Found: ·C, 76.31; H, 7.93.

The furfurylidenecyclohexanone was alkylated with methyl iodide in *t*-butyl alcohol in the presence of potassium *t*-butoxide following the general procedure of Johnson.[7]

2-Furfurylidene-5,6,6-trimethylcyclohexanone (VIII) was obtained as pale yellow tablets, mp 76–77°.

Anal. Calcd for $C_{14}H_{18}O_2$: mol wt, 218. Found: mol wt (mass spectroscopy), 218.

A similar procedure using methyl-d_3 iodide instead of methyl iodide gave the 6-methyl-d_3 analog (VIIIa), mp 76–77°. Alkylation with ethyl iodide gave **2-furfurylidene-5,6-dimethyl-6-ethylcyclohexanone** (XXI) as an unstable yellow gum which failed to crystallize. It was purified by glpc (5-ft silicone rubber, 200°).

Anal. Calcd for $C_{15}H_{20}O_2$; C, 77.55; H, 8.68. Found: C, 77.71; H, 8.62.

Alkylation with ethyl-β-d_3 bromide gave the corresponding **6-ethyl-β-d_3 analog XXIa.**

cis-2-Benzylidene-9-methyl-d_3-1-decalone (Xa) and *cis*-1-Benzylidene-8-methyl-d_3-hydrindan (VIa). 2-Benzylidene-1-decalone (6 g) was added to a suspension of sodium hydride (0.6 g) in dimethoxyethane (50 ml) and the mixture was stirred under nitrogen at room temperature. Trideuteriomethyl iodide (98% d_3 1.76 ml, 10% excess) was added and the mixture was stirred overnight in a nitrogen atmosphere at room temperature. The mixture was then heated under reflux for 1 hr and poured into water (500 ml), and the product was extracted with ether (two 100-ml portions). The ethereal extracts were combined, washed with water (two 100-ml portions), and dried over anhydrous magnesium sulfate, and the ether was removed. The crude product (5.6 g, 87%) was recrystallized once from methanol to give *cis*-2-benzylidene-9-methyl-d_3-1-decalone (Xa) as yellow plates, mp 105–106°. This compound was converted by known procedures[11] into *cis*-8-methyl-d_3-1-hydrindanone, which was shown by glpc (10-ft 10% Carbowax 20M on 60–80 Chromosorb W, 110°) to contain approximately 20% of the corresponding *trans* isomer, arising from *trans* isomer contaminant in the starting material. The Grignard reagent from magnesium (0.155 g, 2 mole equiv) and benzyl chloride (0.82 g, 2 mole equiv) in ether (25 ml) was prepared under nitrogen and stirred during the addition of the above *cis*-8-methyl-d_3-1-hydrindanone (0.5 g, 1 mole equiv) in ether (25 ml). The mixture was refluxed for 4 hr and decomposed with 5% hydrochloric acid (30 ml). The product was extracted into ether, the ether layer was washed and dried over anhydrous magnesium sulfate, and the ether was evaporated. The crude residue was treated with a mixture of pyridine and phosphorus oxychloride (27:18, 25 ml) and left overnight. The reaction mixture was poured onto ice, the product extracted into ether, and the ethereal solution washed with a saturated solution of sodium bicarbonate and dried over anhydrous magnesium sulfate. The ether was removed and the residue purified by glpc (10-ft 10% Apiezon L on 60–80 Chromosorb W, 210°). The following compounds were isolated: (a) 1,2-diphenylethane (identified by comparison of retention times and infrared spectrum with an authentic specimen); (b) *cis*-1-benzyl-8-methyl-d_3-Δ^1-hydrindene (identified by its nmr spectrum (CDCl$_3$), which showed a multiplet at δ 3.33, corresponding to the two benzylic protons, and a multiplet at δ 4.99, corresponding to the single olefinic proton at C-2, and its infrared spectrum showing $\nu_{C=C}$ 1610 cm^{-1}); (c) *cis*-1-benzylidene-8-methyl-d_3-hydrindan [(VIa, identified by its nmr spectrum (CDCl$_3$) which showed a triplet at δ 6.26 ($J = 2.5$ cps), corresponding to one benzylic–allylic proton, and a broad multiplet at δ 2.7, corresponding to the two allylic protons at C-2, and its infrared spectrum showing $\nu_{C=C}$ 1650 cm^{-1}]. In addition, small quantities of the *trans* isomers of the last two compounds were also isolated (the latter having arisen from *trans*-hydrindanone impurity in the starting material). The unlabeled hydrindan VI was prepared in an identical fashion starting with X.

In an analogous sequence 2-furfurylidene-5,6,6-trimethylcyclohexanone gave a mixture of **1-benzylidene-4,5,5-trimethylcyclopentane** (XXIII) and **1-benzyl-4,5,5-trimethyl-Δ^1-cyclopentene** which was separated by glpc (5-ft 10% SE 30 on 60–80 Chromosorb W, 185°).

trans-2-Furfurylidene-9-methyl-1-decalone-3-d_1 (IIIb) and *trans*-2-Benzylidene-9-methyl-1-decalone-3-d_1 (XIb).[15] *trans*-1-Methoxy-

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3-keto-9-methyl-$\Delta^{1,6}$-hexahydronaphthalene[12] (0.5 g) was reduced with lithium aluminum deuteride (0.12 g) in ether (40 ml) for 2 hr. Excess reagent was destroyed with a saturated solution of sodium sulfate and the ether-soluble material was heated with water (2.0 ml) and concentrated sulfuric acid (0.3 ml) at 97° for 2.5 hr. The mixture was cooled and the product was extracted into ether and vacuum distilled, yielding *trans*-1-keto-9-methyl-$\Delta^{2,6}$-hexahydronaphthalene (0.33 g), bp 65–70° (air-bath temperature) (1 mm), as a yellow oil. This product was dissolved in ethyl acetate (20 ml) and hydrogenated over 10% palladium–carbon catalyst at atmospheric pressure until gas absorption ceased (30 min, 42 cc). The catalyst was removed by filtration, the solvent was evaporated, and the residue was distilled (bath temperature 130–140°) at 18 mm to give *trans*-9-methyl-1-decalone-3-d_1 (0.32 g). This decalone (0.06 g) in ethanol (0.6 ml) was treated with 15% aqueous sodium hydroxide solution (0.16 ml) and freshly distilled furfuraldehyde (0.04 ml) was added. After standing at room temperature in the dark for 18 hr, the mixture was filtered and the solid product recrystallized from methanol to afford *trans*-2-furfurylidene-9-methyl-1-decalone-3-d_1 (IIIb) as cream plates, mp 86–87° (λ_{max} 321 mμ (log ϵ 4.36, in ethanol)). The benzylidene derivative (XIa) was obtained as colorless plates, mp 92.5–93.5°, by using benzaldehyde (0.04 ml) instead of furfuraldehyde in the last step.

2-Furfurylidene-5,6-dimethyl-6-phenylcyclohexanone (XXII). A solution of 4,5-dimethyl-4-phenyl-Δ^2-cyclohexenone[5] (2.48 g) in methanol (20 ml) was treated with 30% hydrogen peroxide (5.15 ml). The mixture was cooled to 15° and 6 N caustic soda (1.48 ml) was added dropwise with stirring at 15–17° during 12 min. The mixture was kept at 15–20° for 3 hr, poured into water, and extracted with ether. The ethereal extract was washed and dried over anhydrous magnesium sulfate and the ether evaporated. **4,5-Dimethyl-4-phenylcyclohexanone 2,3-epoxide** was obtained as a colorless oil, ν_{co} 1710 cm^{-1}. The crude epoxy ketone (2 g) was refluxed with 100% hydrazine hydrate (23 ml) containing hydrazine sulfate (7.4 g) for 20 min. The mixture was cooled, diluted with water, and extracted with ether. The ethereal extract was washed and dried over anhydrous magnesium sulfate, and the ether was removed, leaving a viscous brown gum. Distillation at 0.7 mm (bath temperature 150–170°) gave **5,6-dimethyl-6-phenyl-Δ^2-cyclohexenol** (0.6 g) as a pale yellow viscous oil, a portion of which was purified by glpc (10-ft 10% Apiezon L on 60–80 Chromosorb W, 180°).

Anal. Calcd for $C_{14}H_{18}O$: C, 83.12; H, 8.79. Found: C, 83.0; H, 8.90.

Oxidation of the alcohol with excess 8 N Jones reagent[10] in acetone gave after ether extraction **5,6-dimethyl-6-phenyl-Δ^2-cyclohexenone** (0.4 g) as a yellow oil, ν_{co} 1680 cm^{-1}.

Anal. Calcd for $C_{14}H_{16}O$: C, 83.96: H, 8.05. Found: C, 83.67; H, 8.33.

The cyclohexenone (0.32 g) in ethyl acetate (25 ml) was hydrogenated over 10% palladium–carbon catalyst (100 mg) at room temperature and pressure until hydrogen uptake ceased (47 ml). The catalyst was removed and the solvent evaporated, giving **5,6-dimethyl-6-phenylcyclohexanone** as a colorless oil, ν_{co} 1725 cm^{-1}. A portion was purified for analysis by glpc (10-ft 10% Apiezon L on 60–80 Chromosorb W, 175°).

Anal. Calcd for $C_{14}H_{18}O$: C, 83.12; H, 8.79. Found: C, 83.17; H, 9.06.

The cyclohexanone (0.25 g) was dissolved in methanol (5 ml) containing sodium methoxide (0.1 g), and redistilled furfuraldehyde (0.15 g) was added. The mixture was left at room temperature under nitrogen overnight and poured into water, and the product was isolated by ether extraction as usual. **2-Furfurylidene-5,6-dimethyl-6-phenylcyclohexanone (XXII)** (0.3 g) was obtained as a yellow viscous gum which did not crystallize and darkened rapidly on exposure to air. Purification was effected by glpc (5-ft 10% SE30 on 60–80 Chromosorb W, 250°).

Anal. Calcd for $C_{19}H_{20}O_2$: C, 81.40; H, 7.19. Found: C, 81.50: H, 7.26.

2-Furfurylidene-4,5,5-trimethylcyclopentanone (XXIV). 2,2,3-Trimethylcyclopentanone (0.126 g) and redistilled furfuraldehyde (0.096 g) were dissolved in methanol (2 ml), and sodium methoxide (0.050 g) was added. The mixture was left overnight under an atmosphere of nitrogen and poured into water, and the product was isolated by ether extraction and purified by glpc (5-ft SF96, 185°). The product was obtained as an unstable yellow oil which darkened immediately on exposure to air.

Anal. Calcd for $C_{13}H_{16}O_2$: mol wt, 204. Found: mol wt (mass spectroscopy), 204.

Similarly *cis*-8-methyl-d_3-hydrindanone (see above) was condensed with furfuraldehyde to give the **furfurylidene derivative (XIX)** as an unstable viscous yellow gum.

Anal. Calcd for $C_{15}H_{15}D_3O_2$: mol wt, 233. Found: mol wt (mass spectroscopy), 233.

Communications to the Editor

A New Route to the Preparation and Configurational Correlation of Optically Active Phosphine Oxides[1]

Sir:

Optically active phosphine oxides occupy a key position in the stereochemical investigations of phosphorus compounds.[2,3] Produced[3] from optically active quaternary phosphonium salts by reaction with sodium hydroxide, from optically active phosphoranes by the Wittig reaction, or from optically active phosphines by oxidation, phosphine oxides are themselves precursors

(1) This work was supported by the Air Force Office of Scientific Research under Grant No. AF-AFOSR-1188-67.

(2) Resolution of ethylmethylphenylphosphine oxide (5) provided the first example of an optically active phosphorus compound (J. Meisenheimer and L. Lichtenstadt, *Ber.*, 44, 356 (1911); J. Meisenheimer, J. Casper, M. Höring, W. Lauter, L. Lichtenstadt, and W. Samuel, *Ann.*, 449, 213 (1926)).

(3) For comprehensive reviews giving citations to the original literature, see R. F. Hudson and M. Green, *Angew. Chem. Intern. Ed. Engl.*, 2, 11 (1963); L. Horner, *Pure Appl. Chem.*, 9, 225 (1964); W. E. McEwen in "Topics in Phosphorus Chemistry," Vol. 2, M. Grayson and E. J. Griffith, Ed., Interscience Publishers, Inc., New York, N. Y., 1965, Chapter 1; G. Kamai and G. M. Usacheva, *Russ. Chem. Rev.*, 35, 601 (1966).

to optically active phosphines by reduction with trichlorosilane.[4] Present synthetic routes to optically active phosphines ($R_1R_2R_3P$) and phosphine oxides ($R_1R_2R_3PO$) require resolution[2] of the individual phosphine oxides or, more commonly,[3] resolution of quaternary phosphonium salts ($R_1R_2R_3R_4P^+X^-$) with subsequent cleavage, either by cathodic reduction or by reaction with base, to effect the elimination of R_4. Consequently, whatever the method of preparation, the ultimate starting material has to be one in which the three groups, R_1, R_2, and R_3, are already present prior to optical resolution. This structural commitment severely restricts the scope of these methods and limits the pathways which are accessible for configurational intercorrelations, particularly so since, to achieve selective elimination, the ease of cleavage of R_4 must be substantially greater than that of the other three groups.

We have developed a synthetic scheme which overcomes these difficulties. Unsymmetrically substituted

(4) L. Horner and W. D. Balzer, *Tetrahedron Letters*, 1157 (1965).

Chart I[a,b]

a Men = (−)-menthyl; An = p-anisyl; C_3H_7 = n-propyl. b Grignard reactions are described in the text; for other reactions, see ref 3 and 4.

Chart II[a]

a Alk = alkyl group; Ar = aryl group.

menthyl phosphinates ($R_1R_2P(O)OMen$) are readily separated into the diastereomeric forms. Reaction with alkyl or aryl Grignard reagents (R_3MgX) in benzene at 70° affords phosphine oxides[5] ($R_1R_2R_3PO$) with a high degree of stereospecificity. Thus, reaction of methylmagnesium chloride with diastereomerically pure[6] menthyl phenyl-n-propylphosphinate[7] (**1A**, mp 86°, $[\alpha]^{23}D$ −14° (benzene)) gives methylphenyl-n-propylphosphine oxide (**2**), $[\alpha]^{23}D$ +17.3° (methanol);[8] reaction with a mixture consisting of 87.4% of the epimer **1B** (mp 40°, $[\alpha]^{23}D$ −81.3° (benzene)) and 12.7% of **1A** gives **2** with $[\alpha]^{22}D$ −12.7° (methanol) (see Chart I). Since the chirality of the phosphorus atom in **1A** is R,[9] as determined by X-ray analysis,[10] and since the chirality of (+)-**2** is R by correlation[3,4] with (+)-(S)-benzylmethylphenyl-n-propylphosphonium bromide (**3**),[11] it follows that the Grignard reaction proceeds

with inversion of configuration.[12] Similarly, reaction of n-propylmagnesium bromide with diastereomerically pure menthyl methylphenylphosphinate[6] (**4B**, mp 80°, $[\alpha]D$ −94° (benzene)) gives (+)-(R)-**2**, $[\alpha]^{23}D$ +17.1° (methanol);[8] since the reaction proceeds with inversion, the chirality of the phosphorus atom in **4B** is S and in **4A**[13] is R. Consequently, the configurations of all phosphine oxides prepared from **4** by the Grignard displacement reaction can be derived. For example, reaction of ethylmagnesium bromide, benzylmagnesium chloride, and p-anisylmagnesium bromide with **4B** gives, respectively, (+)-(R)-ethylmethylphenylphosphine oxide (**5**), $[\alpha]^{22}D$ +21.1° (water),[14] (+)-(R)-benzylmethylphenylphosphine oxide (**6**), $[\alpha]^{23}D$ +50.9° (methanol),[15] and (+)-(S)-anisylmethylphenylphosphine oxide[6] (**7**), $[\alpha]^{23}D$ −8.4° (methanol). In this manner, the configurations of **2** and **6** have been related by conversion from a *single* precursor (**4B**), whereas previous correlations[3,4] required the independent resolution of two phosphonium salts (**3** and **8**), coupled with a minimum of four reaction steps. The most important feature of the new method is indicated by Chart II, where it is shown that configurations of trialkyl-, dialkylaryl-,

(5) K. D. Berlin and R. U. Pagilagan, *J. Org. Chem.*, **32**, 129 (1967), found that alkyldiphenylphosphine oxides can be obtained by reaction of alkyl diphenylphosphinates with alkyl Grignard reagents.

(6) R. A. Lewis, O. Korpiun, and K. Mislow, *J. Am. Chem. Soc.*, **89**, 4786 (1967).

(7) All new compounds gave elemental analyses (C, H, P) and nmr spectra consistent with their structures. Menthyl esters **1** and **4** were prepared by the conventional route: $C_6H_5PCl_2$ (+ROH) → $C_6H_5P(OR)_2$ (+RI) → $C_6H_5(R)P(O)OR$ (+PCl_5) → (C_6H_5)(R)P(O)Cl (+(−)-menthol) → **1** (R = n-C_3H_7) and **4** (R = CH_3), and the epimers were separated by fractional crystallization.

(8) The highest reported rotation for **2** is $[\alpha]D$ +19.6° (methanol) (D. B. Denney and J. W. Hanifin, Jr., *Tetrahedron Letters*, 2177 (1963)).

(9) In the specification of chirality, contributions by d orbitals to bonds of quadriligand atoms are neglected (R. S. Cahn, C. Ingold, and V. Prelog, *Angew. Chem. Intern. Ed. Engl.*, **5**, 385 (1966)).

(10) Unpublished work by E. B. Fleischer and R. Dewar. We thank Professor Fleischer for communicating these results to us prior to publication.

(11) A. F. Peerdeman, J. P. C. Holst, L. Horner, and H. Winkler, *Tetrahedron Letters*, 811 (1965).

(12) This result is analogous to the inversion accompanying transesterification of methyl ethylphenylphosphinate (M. Green and R. F. Hudson, *J. Chem. Soc.*, 540 (1963)), and to the inversion accompanying reaction of menthyl sulfinates with Grignard reagents (K. K. Andersen, *Tetrahedron Letters*, 93 (1962); P. Bickart, M. Axelrod, J. Jacobus, and K. Mislow, *J. Am. Chem. Soc.*, **89**, 697 (1967)).

(13) The epimer[6] of **4B** (i.e., **4A**) has mp 89°, $[\alpha]D$ −16.3° (benzene).

(14) The highest reported rotation for **5** is $[\alpha]D$ +23.1° (water);[2] cf. also K. F. Kumli, W. E. McEwen, and C. A. VanderWerf, *J. Am. Chem. Soc.*, **81**, 3805 (1959).

(15) L. Horner and H. Winkler, *Tetrahedron Letters*, 3265 (1964), report $[\alpha]D$ +48.8° (methanol) for **6**.

alkyldiaryl-, and triarylphosphine oxides may in principle be correlated *via* the appropriately substituted phosphinates; such correlations have not been possible by previously existing methods. We are currently exploring the scope and ramifications of this scheme.

Olaf Korpiun, Kurt Mislow

Department of Chemistry, Princeton University
Princeton, New Jersey 08540
Received June 27, 1967

Configurational Correlation of Phosphinates by Nuclear Magnetic Resonance and Optical Rotatory Dispersion[1]

Sir:

Menthyl phosphinates are useful precursors in the synthesis of optically active phosphorus compounds.[2] We now report that the nmr and ord spectra of these esters are characteristic of configuration and are thus important adjuncts to the assignment of chirality at phosphorus in this family of compounds.
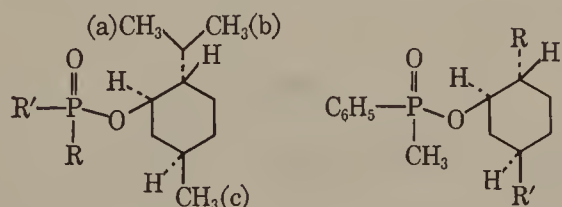
1, R = n-C_3H_7; R' = C_6H_5 5, R = i-C_3H_7; R' = H
2, R = CH_3; R' = C_6H_5 6, R = H; R' = CH_3
3, R = CH_3; R' = C_6H_{11}
4, R = R' = C_6H_5

The absolute configuration of the menthyl esters **1** and **2** has been established.[2] As shown in Table I,

Table I.[a] Pmr Chemical Shifts and Coupling Constants of Phosphinate Esters

| Compd	P–CH_3	H_a	H_b	H_c
			C–CH_3	
1A		9.11 (7.0)	9.05 (7.0)	9.25 (4.5)
1B		9.68 (7.0)	9.19 (7.0)	9.10 (5.0)
2A	8.38 (14.5)	9.11 (7.0)	9.05 (7.0)	9.24 (4.5)
2B	8.14 (14.5)	9.66 (7.0)	9.19 (7.0)	9.11 (5.0)
3A	8.64 (13.0)	9.19 (7.0)	9.08 (7.0)	9.10 (5.0)
3B	8.61 (13.0)	9.19 (7.0)	9.08 (7.0)	9.10 (5.0)
4		9.43 (7.0)	9.12 (7.0)	9.15 (5.0)
5A	8.38 (14.5)	9.10 (7.0)	9.05 (7.0)	
5B	8.32 (14.5)	9.59 (7.0)	9.20 (7.0)	
6A	8.42 (14.5)			Ca. 9.1 (5.0)
6B	8.42 (14.5)			Ca. 9.1 (5.0)

[a] Chemical shifts are given in τ units, and coupling constants (in parentheses) are given in Hz.

the epimers of **1** and **2** having the *S* configuration at phosphorus (**1B** and **2B**) exhibit a downfield shift of the H_c doublet and an upfield shift of the isopropyl doublets (H_a and H_b), relative to the corresponding signals for the epimers which have the *R* configuration at phosphorus (**1A** and **2A**). The large upfield shift of the H_a doublet (*ca.* 0.5 ppm) is particularly striking; its location in a region unencumbered by other signals provides an excellent measure of diastereo-

(1) This work was supported by the Air Force Office of Scientific Research under Grant No. AF-AFOSR-1188-67.
(2) O. Korpiun and K. Mislow, *J. Am. Chem. Soc.*, **89**, 4784 (1967).

meric purity since contamination of **A** by **B** can be easily detected and estimated quantitatively.

The source of the shift experienced by H_a is traceable to the diamagnetic anisotropy of the phenyl ring rather than of the phosphoryl group, as shown by two observations. First, the C–CH_3 protons of the diastereomeric menthyl cyclohexylmethylphosphinates (**3**)[3,4] are indistinguishable at 60 MHz; second, the large upfield shift of H_a is also exhibited by menthyl diphenylphosphinate (**4**).[3] The C–CH_3 proton signals can be assigned by comparison (Table I) of the nmr spectra of esters containing portions of the menthyl group (**5** and **6**) with the spectra of **1–4**. First, both diastereomers of racemic *trans*-2-isopropyl-1-cyclohexyl methylphenylphosphinate (**5**)[3] feature two C–CH_3 doublets with $J = 7.0$ Hz; second, **5B** exhibits a 0.5-ppm upfield shift of one doublet relative to the corresponding signal in **5A**; third, both diastereomers of *cis*-3-methyl-1-cyclohexyl methylphenylphosphinate (**6**)[3] exhibit a C–CH_3 doublet with $J = 5.0$ Hz. Consequently, H_a must be located in the isopropyl portion of **1–5** and is diagnostic of configuration. For example, given the 1R,2S,5R configuration of menthol,[5] it can be deduced that **5A** is a mixture of enantiomers, one of which has the R configuration at phosphorus and the 1R,2S configuration in the cyclohexyl moiety, *i.e.*, $(R)_P$-(1R,2S)$_C$, while the other has the $(S)_P$-(1S,2R)$_C$ configuration; similarly **5B** is an equimolar mixture of $(S)_P$-(1R,2S)$_C$ and $(R)_P$-(1S,2R)$_C$ enantiomers.

The remaining question is to decide which of the two diastereotopic[6] methyl groups in the isopropyl portion of **1–5** is associated with the most highly shielded proton, H_a. If we assume minimal conformational strain in the menthol portion and an "up" conformation for the phosphinate ester grouping,[7] the most populated conformation of **1–4** (and, by extension, **5**) may be represented by stereoformula **7**. If this formulation is correct, it follows that when R' = phenyl, as in **1B**, **2B**, **4**,

7
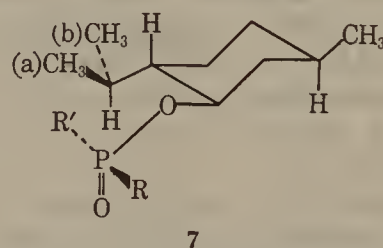
and $(S)_P$-(1R,2S)$_C$-**5**, the more highly shielded proton (H_a) is located on the methyl group which has the *pro-R* chirality[8,9] and the less highly shielded proton (H_b) on the methyl group which has the *pro-S* chirality.[8]

(3) All new compounds gave elemental analyses (C, H, and P) and nmr spectra consistent with their structures.
(4) Prepared from $C_6H_{11}P(Cl)N(C_2H_5)_2$ (K. Issleib and W. Seidel, *Chem. Ber.*, **92**, 2681 (1959)) by the route (+CH_3OH) → $C_6H_{11}P(OCH_3)_2$ (+CH_3I) → $(C_6H_{11})(CH_3)P(O)OCH_3$ (+PCl_5) → $(C_6H_{11})(CH_3)P(O)Cl$ (L. Z. Soborovskij and J. M. Zinovjev, *Zh. Obshch. Khim.*, **24**, 516 (1954)), followed by reaction with (−)-menthol and separation of the epimers by fractional crystallization.
(5) V. Prelog, *Helv. Chim. Acta*, **36**, 308 (1953).
(6) K. Mislow and M. Raban in "Topics in Stereochemistry," Vol. I, N. L. Allinger and E. L. Eliel, Ed., John Wiley and Sons, Inc., New York, N. Y., 1967, Chapter 1.
(7) T. H. Siddall, III, and C. A. Prohaska, *J. Am. Chem. Soc.*, **84**, 3467 (1962); K. D. Berlin and R. U. Pagilagan, *Chem. Commun.*, 687 (1966); K. D. Berlin and R. U. Pagilagan, *J. Org. Chem.*, **32**, 129 (1967).
(8) K. R. Hanson, *J. Am. Chem. Soc.*, **88**, 2731 (1966).
(9) Similar arguments have been advanced by T. S. Sorensen, *Can. J. Chem.*, **45**, 1585 (1967), in a discussion of the nmr spectra of isopropylcyclopentenones.
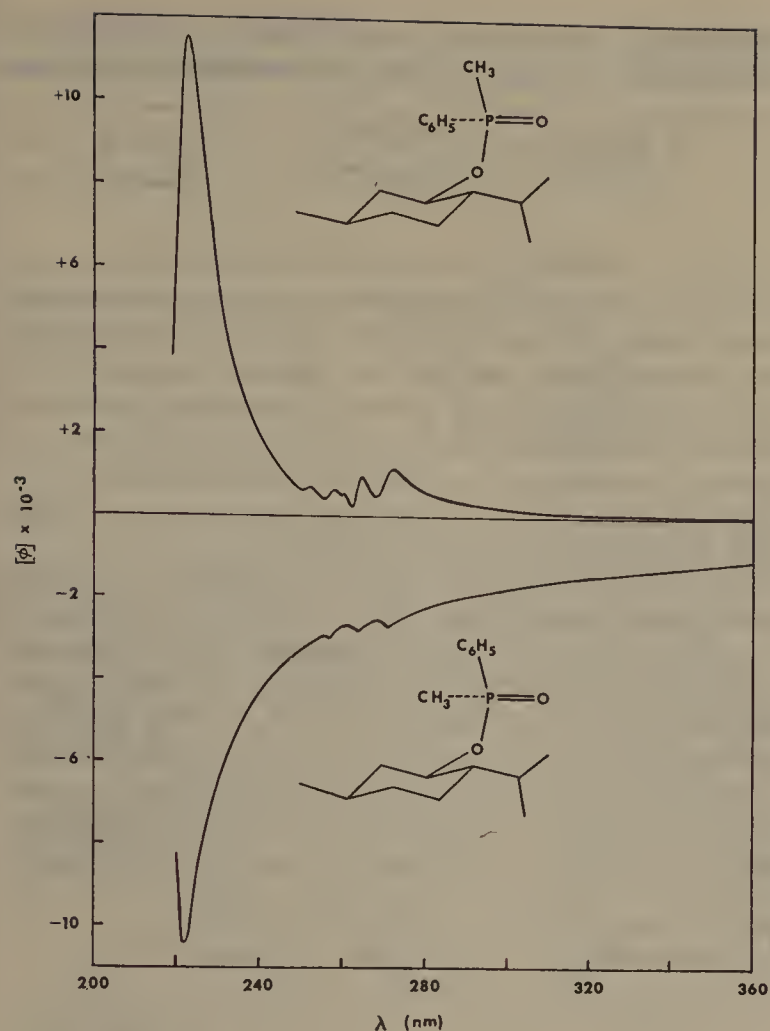
Figure 1.

The ord curves (Figure 1) of **2A** and **2B** are enantiomeric in type, the positive and negative Cotton effects corresponding to the R and S configurations at phosphorus, respectively. The chirality of the benzenephosphoryl chromophore (λ_{max} 210 nm (ϵ 8300), 217 nm (ϵ 7800)) dominates the ord, as previously found[10] for the analogous p-iodobenzenesulfinyl chromophore in the diastereomeric menthyl p-iodobenzenesulfinates. Further studies on the correlation of configuration and ord of phosphinates and phosphine oxides[11] are in progress.

(10) K. Mislow, M. M. Green, P. Laur, J. T. Melillo, T. Simmons, and A. L. Ternay, Jr., *J. Am. Chem. Soc.*, **87**, 1958 (1965).
(11) See also L. Horner and H. Winkler, *Tetrahedron Letters*, 3265 (1964); O. Červinka and O. Kříž, *Collection Czech. Chem. Commun.*, **31**, 1910 (1966).
(12) U. S. Public Health Service Predoctoral Fellow, 1966–1967.

Robert A. Lewis,[12] Olaf Korpiun, Kurt Mislow
Department of Chemistry, Princeton University
Princeton, New Jersey 08540
*Received June 27, 1967*

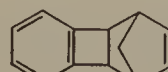## Oxidative Degradation of (Benzocyclobutadiene)iron Tricarbonyl

Sir:

Previous work by Cava[1] and by Nenitzescu[2] and their collaborators has indicated that benzocyclobutadiene (I) is produced upon dehalogenation of dihalobenzocyclobutene with zinc or lithium amalgam. When

(1) M. P. Cava and D. R. Napier, *J. Am. Chem. Soc.*, **79**, 1701 (1957).
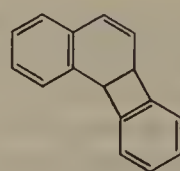
conducted in the presence of cyclopentadiene, this reaction produces the Diels–Alder adduct II whereas, in the absence of added diene, the hydrocarbon III is formed.[2,3] Compound III is reasoned to be the stable rearrangement product of the intermediate Diels–Alder type dimer of benzocyclobutadiene.
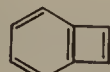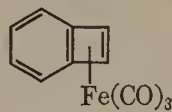

Our previous studies have indicated that cyclobutadiene is liberated upon oxidative degradation of cyclobutadieneiron tricarbonyl.[4] However, as also reported earlier, oxidative decomposition of (benzocyclobutadiene)iron tricarbonyl (IV) using silver ions as the oxidant produced none of the normal dimerization product of I, *viz.* III, but instead gave rise to the isomeric hydrocarbon V;[5] oxidation with ceric ion produced polymeric material. This has then raised the important question as to whether free benzocyclobutadiene is liberated in these oxidative decompositions. In this paper we wish to report evidence indicating that I is indeed produced upon oxidation of IV and to rationalize the anomaly presented by the formation of V.

It is now found that oxidative degradation of the complex IV in the presence of cyclopentadiene, using lead tetraacetate in pyridine, produces the hydrocarbon II identical with an authentic sample prepared by the method of Nenitzescu.[2] In the absence of cyclopentadiene this oxidation also produces the normal dimer III in good yield, and none of the isomeric compound V can be detected. Identical behavior is found when ferric nitrate in aqueous ethanol is used as the oxidant. These products parallel exactly the pattern found in the earlier dehalogenation reactions and support the contention that the benzocyclobutadiene is implicated in their formation.

The rate of oxidation of the complex IV is fast and appears to be comparable to that of the oxidation of cyclobutadieneiron tricarbonyl with Pb(OAc)$_4$. Since evidence indicated benzocyclobutadiene to be reactive as a dienophile but not as a diene,[3] this then suggested the intriguing possibility of being able to add cyclobutadiene to benzocyclobutadiene by this technique. This has now proved to be possible; addition of a mixture of cyclobutadieneiron tricarbonyl and the complex IV to Pb(OAc)$_4$ afforded the adduct VI[6] in 75% yield.

(2) C. D. Nenitzescu, M. Avram, and D. Dinu, *Chem. Ber.*, **90**, 2541 (1957).
(3) M. P. Cava and M. J. Mitchell, *J. Am. Chem. Soc.*, **81**, 5409 (1959).
(4) J. C. Barborak and R. Pettit, *ibid.*, **89**, 3080 (1967), and references therein.
(5) G. F. Emerson, L. Watts, and R. Pettit, *ibid.*, **87**, 131 (1965).
(6) White crystalline solid, mp 17°, nmr absorptions at τ 2.98, 4.28, 6.22–6.77, having areas of 4:2:4, respectively. Elemental analysis and molecular weight are in agreement with the formula $C_{12}H_{10}$.

Compound VI undergoes thermal isomerization to benzocyclooctatetraene in almost quantitative yield.[7]
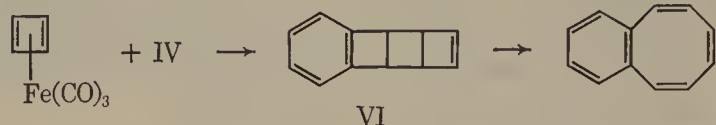
The question raised by the formation of the hydrocarbon V in the degradation with Ag+ now clearly implicates involvement (other than mere oxidation) by the silver ion. Confirmation of this is seen in the fact that whereas degradation of IV with ferric nitrate gives only the normal dimer III, when the same oxidation is conducted in the presence of catalytic amounts of silver nitrate (20 molar %) the sole $C_{16}H_{12}$ product is V. Under a variety of conditions we have not been able to effect the isomerization of III to V with silver ion; hence III cannot be the precursor of V. The remarkable facile silver ion catalyzed isomerization of strained benzocyclobutenes to o-xylylenes discussed in the accompanying paper[8] now suggests a reasonable role for Ag+. The dimerization of I produces the unstable Diels–Alder adduct VII which, before it thermally isomerizes to the normal dimer III, could undergo silver ion catalyzed rearrangement to the o-xylylene derivative
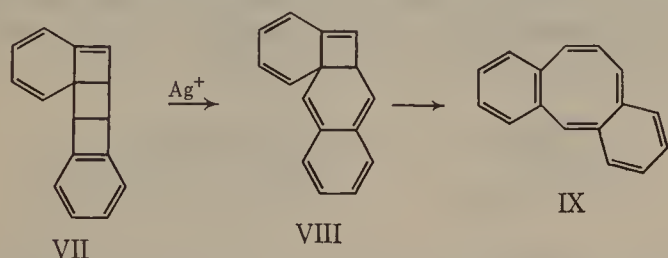
VIII and thence to the cyclooctatetraene derivative IX. Intramolecular Diels–Alder addition of IX would then produce the hydrocarbon V.

(7) The product has properties identical with those reported by G. Wittig, H. Eggers, and P. Duffner, *Ann.*, **619**, 10 (1958).

(8) W. Merk and R. Pettit, *J. Am. Chem. Soc.*, **89**, 4788 (1967).

(9) We thank the National Science Foundation, The U. S. Army Research Office (Durham), and the Robert A. Welch Foundation for financial support. We also thank Badische Anilin and Soda Fabrik and General Aniline and Film Corp. for generous gifts of cyclooctatetraene and iron carbonyl, respectively.

W. Merk, R. Pettit[9]

Department of Chemistry, The University of Texas
Austin, Texas 78712

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Metal Ion Catalyzed Cyclobutene–Butadiene and Benzocyclobutene–o-Xylylene Isomerizations

Sir:

We wish to report examples of facile metal ion (Ag+ and Cu+) catalyzed isomerizations of derivatives of cyclobutene to those of butadiene. Of particular interest in these reactions is the fact that if they proceed in a concerted manner they must do so by means of a disrotatory process.

Nenitzescu and co-workers have reported that *anti*-tricyclooctadiene (I) isomerizes to cyclooctatetraene with a half-life of 20 min at 140°.[1] We have found that,

(1) M. Avram, I. G. Dinulescu, E. Marica, G. Mateescu, E. Sliam, and C. D. Nenitzescu, *Chem. Ber.*, **97**, 382 (1964).

in the presence of silver fluoroborate, the half-life is 5 min at 56°. A solution of I with equimolar amounts
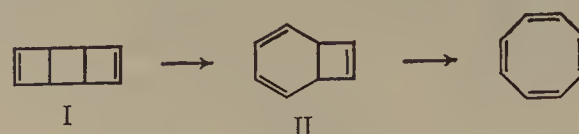
of $AgBF_4$ in boiling acetone is completely isomerized to cyclooctatetraene within 40 min; under the same conditions, in the absence of the silver salt, there is practically no isomerization after 24 hr. Similar rate enhancements are observed in acidified methanolic solutions containing cuprous chloride. Because of the *trans* nature of the rings in I, a one-step isomerization to cyclooctatetraene seems highly improbable; the initial step more likely involves the triene II.

The effect of silver ion is most dramatic in the case of dibenzotricyclooctadiene (III). This hydrocarbon is reported to undergo thermal isomerization to dibenzocyclooctatetraene (V) upon heating in refluxing o-dichlorobenzene (bp 180°) for 4–5 hr.[2] We find that at room temperature, in tetrahydrofuran in the presence of molar quantities of $AgBF_4$, the isomerization is complete within 10 sec. A solution of III in the absence of silver ion reveals no detectable (nmr) isomerization
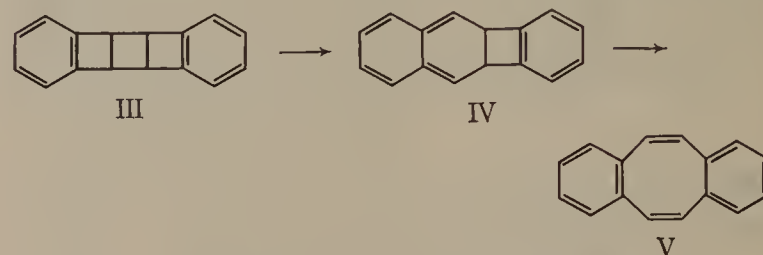
after standing at room temperature for 1 week.

When the hydrocarbon III is slowly added to a solution of $AgBF_4$ and maleic anhydride in ether at room temperature, the Diels–Alder adduct VI[3] is produced in high yield. Compound VI is not produced when maleic anhydride is added at room temperature to V, with or without added $AgBF_4$, or to compound III alone. This strongly suggests that the silver ion catalyzed isomerization of III proceeds *via* the o-xylylene derivative IV.
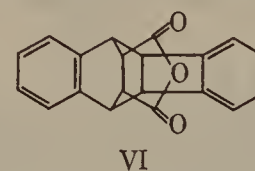
A further interesting case is afforded by benzotricyclooctadiene (VII).[4] Addition of $AgBF_4$ to an ethereal solution of VII at 25° produces an almost instant precipitate of the silver complex of benzocyclooctatetraene; decomposition of the complex with NaCl affords benzocyclooctatetraene in better than 90% over-all yield. Again a solution of VII shows no detectable isomerization upon standing at 25° for several days. Addition of VII to maleic anhydride and $AgBF_4$ in ether at 25° produces the Diels–Alder adduct X.[5] This indicates that the catalyzed rearrangement of VII involves first a benzocyclobutene–o-xylylene re-

(2) M. Avram, D. Dinu, G. Mateescu, and C. D. Nenitzescu, *ibid.*, **93**, 1789 (1960).

(3) M. Avram, I. G. Dinulescu, D. Dinu, G. Mateescu, and C. D. Nenitzescu, *Tetrahedron*, **19**, 309 (1963).

(4) W. Merk and R. Pettit, *J. Am. Chem. Soc.*, **89**, 4787 (1967).

(5) The nmr spectrum of this adduct confirms the structure indicated.

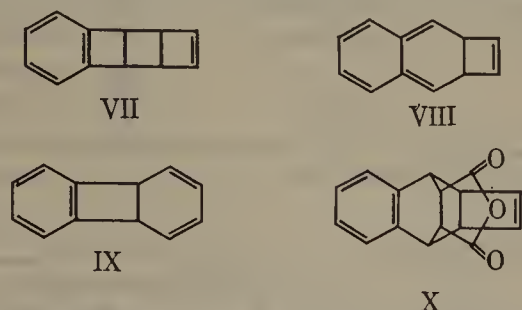arrangement to give VIII as an intermediate rather than a cyclobutene–butadiene rearrangement involving compound IX. Again, addition at room temperature of maleic anhydride to either benzocyclooctatetraene or to compound VII produces none of the adduct X.

VII

VIII

IX

X

The isomerizations of compounds I, III, and VII would be expected to be exothermic reactions. The compounds owe their stability in part to the fact that the cyclobutene–butadiene transformations and, as can be shown by analogous reasoning, the benzocyclobutene–o-xylylene isomerizations are expected by the Woodward–Hoffmann rules to be conrotatory processes.[6] In these instances such rotations cannot occur because of constraints imposed by the nature of the rings to be formed. One possible explanation for the role of the metal ion in the isomerizations is that they allow the concerted disrotatory process to proceed via intermediate metal π complexes. Extension of the arguments given by Longuet-Higgins and Abrahamson[7,8] for the cyclobutene ring opening, applied to the isomerization of the cyclobutene–cuprous complex XI to the butadiene–cuprous complex XII, offers support of this.

XI XII XIII XIV
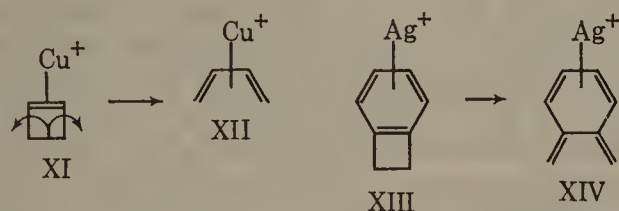
The symmetry of the appropriate orbitals of cyclobutene, butadiene, and the metal ion (Cu⁺ or Ag⁺), respectively, in the disrotatory process are as indicated: symmetrical, σ, π; ψ_1, ψ_3; s, $p_y, p_z, d_{yz}, d_{z^2}$; antisymmetrical, σ^*, π^*; ψ_2, ψ_4; p_x, d_{xy}, d_{xz}.

A satisfactory description[9] of the ground state of complex XI will be $\sigma^2, (\pi, s-d_{z^2})^4, (\pi^*, p_x-d_{xz})^2, (p_y-d_{yz})^2, d_{xy}^2$. From the orbital classification listed, it is seen that the disrotatory process leading to an electron configuration $(\psi_1, s-d_{z^2})^4, (\psi_2, p_x-d_{xz})^2, (\psi_3, p_y-d_{yz})^4, (\psi_4, d_{xy})^2$ is an allowed process and, according to qualitative concepts, this latter should represent a stable configuration of the complex XII.[10] Analogous arguments can be derived for the disrotatory process of the benzocyclobutene complex XIII, giving the o-xylylene complex XIV.

(6) R. B. Woodward and R. Hoffmann, *J. Am. Chem. Soc.*, **87**, 395 (1965).

(7) H. C. Longuet-Higgins and E. W. Abrahamson, *ibid.*, **87**, 2045 (1965).

(8) Similar applications of these concepts have recently been applied by F. D. Mango and J. H. Schachtschneider [*ibid.*, **89**, 2484 (1967)] in consideration of metal-catalyzed intermolecular cyclization reactions.

(9) M. J. S. Dewar, *Bull. Soc. Chem. France*, **18**, C79 (1951).

(10) It is to be noted that the over-all change in symmetry involved in the cyclobutene–butadiene conversion, namely $\sigma^2\pi^2$ (SS) to $\psi_1^2\psi_2^2$ (SA), which is forbidden in the absence of metal ion, becomes compensated through a similar change in the metal ion configuration $(p_x-d_{xy})^2$ (A) to $(p_y-d_y)_z^2$ (S).

We then propose that the role of the metal ion is to form an organometallic complex in which the sterically preferred disrotatory isomerization process is now allowed, the driving force for the reaction being relief of internal strain. Further investigation of these types of isomerizations are in progress.

W. Merk, R. Pettit[11]
Department of Chemistry, The University of Texas
Austin, Texas 78712

Steroids. CCCXIII. Electrochemical Reactions. I. Reduction of Carbonyl Functions to Methylene or Deuteriomethylene Analogs

Sir:

The cathodic reduction of carbonyl compounds has been studied extensively and several review articles are available in the literature concerning this process.[1] Depending mainly on the electrode potential, the nature of the electrode, and the pH of the electrolyte, the reduction products can be alcohols (I), pinacols (II) and their subsequent rearrangement products, or hydrocarbons (III).

$R_2C=O$

2e/mole

1e/mole

4e/mole

R_2CH
|
OH

I

$R_2-C-C-R_2$
| |
$OH\ OH$

II

R_2CH_2

III
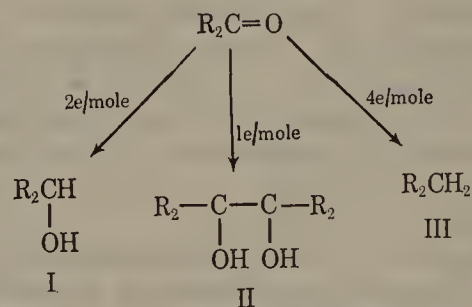
The synthetic scale electrochemical reduction of non-conjugated steroidal ketones and α-ketols at a stirred mercury cathode was found to yield the thermodynamically more stable equatorial alcohols with a high degree of stereospecificity and in very good yields.[2] We now wish to report an electrochemical method which provides an easy and efficient way of converting steroidal carbonyl compounds to the corresponding hydrocarbons in acidic medium. Furthermore, by using the appropriate solvent system during the electrolysis, deuterium atoms can be inserted into the molecule in place of the carbonyl group, a labeling technique which is indispensable in modern reaction mechanistic and spectroscopic studies.[3]

These reductions were carried out on samples varying in size from 10 mg to 3 g. The required reduction time was usually from 2 to 8 hr. Generally a 100–200-mg sample was dissolved in 30 ml of reagent grade dioxane; then 30 ml of 10% sulfuric acid was added and the resulting solution was placed into the cathode compart-

(1) M. J. Allen, "Organic Electrode Processes," Reinhold Publishing Corp., New York, N. Y., 1958, Chapter 6; F. D. Popp and H. P. Schultz, *Chem. Rev.*, **62**, 19 (1962); N. Ya. Fioshin, *Usp. Khim.*, **32**, 60 (1963); S. Wawzonek, *Science*, **155**, 39 (1967).

(2) P. Kabasakalian, J. McGlotten, A. Basch, and M. D. Yudis, *J. Org. Chem.*, **26**, 1738 (1961).

(3) For a brief summary of deuterium-labeling techniques see H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Structure Elucidation of Natural Products by Mass Spectrometry," Vol. 1, Holden-Day, Inc., San Francisco, Calif., 1964, Chapter 2.

Table I. Electrochemical Reduction of Carbonyl Compounds in Strongly Acidic Medium

Starting material	Product	Mp, °C	Yield, %	Electrolysis time, hr
17β-Hydroxy-5α-androstan-3-one	5α-Androstan-17β-ol	162–164	97	3.5
3-Methoxy-1,3,5(10)-estratrien-17-one	3-Methoxy-1,3,5(10)-estratriene	77.5–78.5	94	20
17α,20:20,21-Bismethylenedioxy-3β-acetoxypregn-5-en-19-one	17α,20:20,21-Bismethylenedioxy-3β-hydroxypregn-5-ene[a]	242–245	90	4
3β-Hydroxypregn-5-en-20-one	3β-Hydroxypregn-5-ene	133–134	96	5.5
3β,17α-Dihydroxypregn-5-en-20-one	3β-Hydroxypregn-5-ene	133–134	85	6

[a] The product was hydrolyzed by heating it with sodium hydroxide in methanol to yield the free alcohol.

Table II. Deuterium Incorporation by Electrochemical Reduction of Carbonyl Compounds

Starting material	Product	Mp, °C	Isotope composition,[a] %					
			d_0	d_1	d_2	d_3	d_4	d_5
Estrone	Estra-1,3,5(10)-trien-3-ol-17,17-d_2	133–135		6	89	5		
Estrone-16,16-d_2 methyl ether[b]	3-Methoxy-1,3,5(10)-estratriene-16,16-d_2	76–78		6	94			
3β-Hydroxypregn-5-en-20-one	Pregn-5-en-3β-ol-20,20-d_2	134–136		4	84	11	1	
17β-Hydroxy-5α-androstan-3-one	5α-Androstan-17β-ol-3,3-d_2 acetate[c]	80–81.5		1	33	34	25	7
17α,20:20,21-Bismethylenedioxy-3β-acetoxypregn-5-en-19-one	17α,20:20,21-Bismethylenedioxy-3β-acetoxypregn-5-ene-19,19-d_2	170–172	1	6	93			
5α-Cholest-22-en-16-one[d]	5α-Cholest-22-ene-16,16-d_2	96.5–97.5		7	90	3		

[a] The isotope composition was determined mass spectrometrically. [b] The deuterium exchange was carried out by heating under reflux for 48 hr a solution of estrone methyl ether in 90% tetrahydrofuran and 10% deuterium oxide containing a drop of 10% sodium deuterioxide in deuterium oxide. Isotope composition: 5% d_1 and 95% d_2. The reduction was carried out in a protic medium. [c] The reduction product was acetylated with acetic anhydride in pyridine to facilitate purification. [d] This reaction was carried out by Dr. S. G. Wyllie at the Chemistry Department, Stanford University.

ment of the cell.[4] The same electrolyte was used in the anode compartment. The cell was kept at room temperature, the cathode compartment was magnetically stirred, and the current was kept constant at 200 ma. The progress of the reduction was followed by spot testing the reaction mixture directly on thin layer chromatographic plates.

The reduction of some typical steroidal ketones to their methylene analogs proceeded in high yield (see Table I). The thermodynamically more stable alcohol epimer[2] is usually observed as a minor side product (ca. 5%). These alcohols resisted further reduction under the same reaction conditions and, therefore, are not reaction intermediates. The observed reductive cleavage of the hydroxyl function α to the carbonyl group in 3β,17α-dihydroxypregn-5-en-20-one (see Table I) is in agreement with the observations of Kabasakalian, et al.[2] Other hydroxyl groups are unaffected.

Incorporation of two deuterium atoms in place of the carbonyl group can be achieved with a high degree of isotopic purity (see Table II). This method[5] provides an easy means of labeling certain positions on the steroid nucleus, such as the C-17,[6,7] C-19,[8] and C-20[6] positions, which have proven difficult to attain by the ap-

plication of the usual chemical reaction sequences. Deuterium exchange of the enolizable protons α to the carbonyl groups appears to be the major cause of isotopic impurity and it is more pronounced for ketones such as at C-3, for example, for which the enolization is extremely rapid. This technique can also be employed to introduce deuterium atoms onto the carbon atoms adjacent to the carbonyl group by exchanging the enolizable protons with deuterium atoms, followed by the cathodic reduction of the carbonyl group in a protic medium (see the entry for estrone-16,16-d_2 methyl ether in Table II).

Examination of the scope of this reaction and its extention to α,β-unsaturated ketones and other functionalities is currently in progress.

Lewis Throop, László Tökés
*Institute of Steroid Chemistry, Syntex Research
Palo Alto, California 94304*

(4) The electrolyses were performed in a divided cell equipped with a cellulose dialysis membrane. The electrodes were cut from a 1.5-mm-thick lead sheet.

(5) The deuterium-labeled hydrocarbons were prepared in a microcell by using 6 ml of reagent grade dioxane and 6 ml of 10% deuteriosulfuric acid in deuterium oxide (deuterium content 97%) in both compartments. In order to prevent isotope dilution by atmospheric moisture, the air spaces in the cells were flushed with a slow current of dry nitrogen.

(6) C. Djerassi and L. Tökés, *J. Am. Chem. Soc.*, **88**, 536 (1966).

(7) An improved method for the preparation of androstane-17,17-d_2 via the lithium aluminum deuteride reduction of the p-toluenesulfonylhydrazone of the 17-ketone was reported by L. Tökés, Ph.D. Dissertation, Stanford University, 1965.

(8) C. Djerassi and M. A. Kielczewski, *Steroids*, **2**, 125 (1963); R. H. Shapiro, D. H. Williams, H. Budzikiewicz, and C. Djerassi, *J. Am. Chem. Soc.*, **86**, 2837 (1964).

The Radiation Cross-Linking of Hydrogenated Polyethylene[1]

Sir:

Cross-linking of linear polyethylene induced by high-energy irradiation has been shown to be dependent on both the sample temperature and level of crystallinity.[2–4] In particular, it was concluded from the

(1) This work was supported by the National Aeronautics and Space Administration under Research Grant NSG 247-62 to Florida State University.

(2) R. Kitamaru, L. Mandelkern, and J. Fatou, *J. Polymer Sci.*, **2B**, 511 (1964).

(3) R. Kitamaru and L. Mandelkern, *J. Am. Chem. Soc.*, **86**, 3529 (1964).

(4) T. Okada and L. Mandelkern, Abstracts, International Symposium on Macromolecular Chemistry, Tokyo, 1966; *J. Polymer Sci.*, in press.

partitioning between sol and gel of samples identically irradiated at 130–133° that the efficiency of cross-linking of crystalline polyethylene was twice that for a molten or completely amorphous sample.[2,3] It was further determined that $G(H_2)$ was only weakly dependent on the level of crystallinity, implying that the state-dependent cross-linking mechanism proceeds without hydrogen evolution. This avenue for cross-linking implicates end groups in the reactions involved[5] since there is one vinyl end group per molecule for the type of polyethylene usually studied. The role of vinyl groups in highly crystalline samples cannot be appropriately studied by examining fractions of increasing molecular weight inasmuch as the crystallinity content of linear polyethylene above 2–3 $\times$ 10[5] is sharply reduced.[6,7] Completely amorphous and highly crystalline samples of high molecular weight could not be contrasted, therefore, under identical irradiation conditions.

To circumvent this difficulty we have removed the vinyl end group from a lower molecular weight sample by hydrogenation.[8] The hydrogenation was performed on a molecular weight fraction having a viscosity-average molecular weight[6] of 6.1 $\times$ 10[4]. The concentration of vinyl end groups in this sample was 2.17 $\times$ 10^{-5} mole/g, which corresponds to a number-average molecular weight of 4.6 $\times$ 10[4]. After hydrogenation, the viscosity-average molecular weight remained unchanged. The infrared absorption band at 908 cm^{-1}, typical of the vinyl group, had completely disappeared. Both a hydrogenated and unhydrogenated sample was isothermally crystallized from the melt at 130° for 25 days and then slowly cooled to room temperature. The densities of the samples were 0.980 and 0.981 and the enthalpies of fusion were 58.5 and 60.4 cal/g, respectively. These values correspond to a crystalline fraction of about 0.90[6,7] and indicate that both the hydrogenated and unhydrogenated samples possessed identical crystallinity properties.

A comparison of the results of irradiating these samples at 130° in both the highly crystalline and completely molten (amorphous) states is summarized in Table I. For the nonhydrogenated control sample the results are virtually identical with those previously reported.[2-4] The critical dosage required for gelation is about twice as great for the completely amorphous sample as compared to the highly crystalline one. On the other hand, for the hydrogenated sample treated in exactly the same manner, the highly crystalline sample required a slightly higher critical dose for gelation than did the completely amorphous polymer. It becomes clear, therefore, that the greater efficiency of cross-linking in the nonhydrogenated highly crystalline sample must result from reactions involving the vinyl end group. This would be an additional unique cross-linking reaction resulting from irradiation, which involves the vinyl end group in the highly crystalline polymer and does not necessarily require the production of hydrogen. The importance of the vinyl end group in the chemical acts involved and in the possible alteration of the molecular weight distribution have been pointed out by Dole and collaborators.[5,9] Since the end groups are excluded from the crystal lattice,[10] the effective vinyl group concentration is much greater than the nominal concentration. The $G(H_2)$ values for the two highly crystalline polymers are virtually the same. On the other hand, we note that the $G(H_2)$ value of 6.2 for the completely amorphous hydrogenated samples is identical with the asymptotic value obtained for nonhydrogenated high molecular weight material.[4]

In Figure 1 we have plotted the weight fraction sol, W_s, as a function of the ratio of the radiation dose to the critical dosage for gelation. The solid line is calculated according to the theoretical relation[11,12]

$$\frac{-\ln W_s}{1 - W_s} = \frac{R}{R_c} \qquad (1)$$

which is applicable to the cross-linking of molecular weight fractions in the absence of chain scission. Except for the nonhydrogenated highly crystalline sample, the data are in very good accord with the theoretical expectations and rule out any complication from chain scission and intramolecular cross-linking during the

Figure 1. Plot of W_s against the ratio of the radiation dose to the critical dosage required for incipient gelation. Irradiation was carried out at 130°. Nonhydrogenated sample highly crystalline, O; completely amorphous, ●. Hydrogenated sample highly crystalline, △; completely amorphous, ▲.

Table I. Results of the Irradiation of Hydrogenated and Nonhydrogenated Polyethylene at 130°[a]

Sample		R_c[b]	$G(H_2)$[c]
Nonhydrogenated	Completely amorphous	3.1	5.4
	Highly crystalline	1.6	5.6
Hydrogenated	Completely amorphous	4.2	6.2
	Highly crystalline	4.5	5.7

[a] $M_\eta = 6.1 \times 10^4$, $M_n = 4.6 \times 10^4$. [b] Critical dosage in Mrads for gelation at 130°. [b] G value for hydrogen evolution at 130° for irradiation dose of 1.7 Mrads.

(5) M. Dole, D. C. Milner, and T. F. Williams, *J. Am. Chem. Soc.*, **79**, 4809 (1957); **80**, 1580 (1958).
(6) J. Fatou and L. Mandelkern, *J. Phys. Chem.*, **69**, 417 (1965).
(7) L. Mandelkern, *J. Polymer Sci.*, **15C**, 129 (1966).
(8) The hydrogenation, in decalin solution using a rhodium on carbon catalyst, was performed for us by Dr. T. W. Brooks, of Peninsular ChemResearch, Inc. The assistance of Dr. Brooks is gratefully acknowledged.
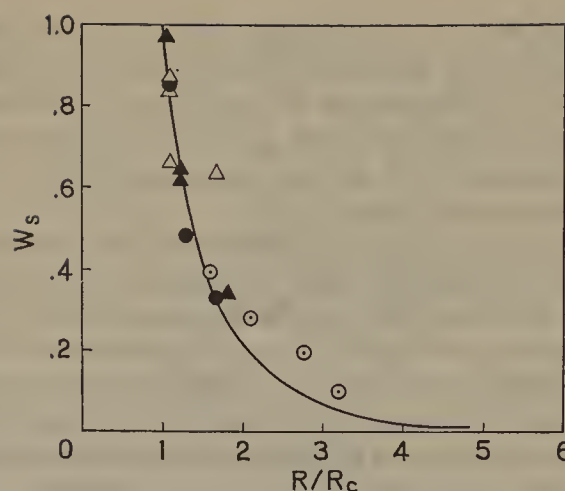(9) M. Dole, M. B. Fallgatter, and K. Katsuuro, *J. Phys. Chem.*, **70**, 62 (1966).
(10) L. Mandelkern, "Crystallization of Polymers," McGraw-Hill Book Co., Inc., New York, N. Y., 1964.
(11) P. J. Flory, *J. Am. Chem. Soc.*, **63**, 3096 (1941).
(12) W. H. Stockmayer, *J. Chem. Phys.*, **12**, 125 (1944).

irradiation.[13] The deviations observed at the higher dosages for the nonhydrogenated, highly crystalline polymer can be attributed to there being more than one cross-linking reaction with a retardation developing in the production of gel as the concentration of vinyl groups becomes depleted.

We can conclude that the enhanced cross-linking efficiency that is observed in the usual crystalline polyethylene is a real effect and not a consequence of any experimental artifacts.[13] The close similarity in cross-linking efficiency between the crystalline and amorphous polymer in the absence of the vinyl end group indicates that this enhancement is a unique and specific chemical effect and would not be generally expected in other crystalline polymers.

(13) M. Dole and K. Katsuura, *J. Polymer Sci.*, 3B, 467 (1965).

T. Okada, L. Mandelkern, R. Glick
Department of Chemistry and Institute of Molecular Biophysics
Florida State University, Tallahassee, Florida 32306
Received April 26, 1967

The Crystal Structure of Twinned Tetrarhodium Dodecacarbonyl[1,2]

Sir:

Although the molecular structures of $Co_4(CO)_{12}$[3] and $Ir_4(CO)_{12}$[4] have recently been completely characterized in the solid state, little structural information has been reported for the presumed tetranuclear metal carbonyl of the congener element rhodium. A structure similar to that of $Co_4(CO)_{12}$ was suggested by Beck and Lottes[5] for the reddish orange $[Rh(CO)_3]_n$ (first prepared by Hieber and Lagally[6]) on the basis of its volatility, diamagnetism, and the resemblance of its *solution* infrared spectrum with that of $Co_4(CO)_{12}$. A three-dimensional X-ray investigation of the rhodium complex was undertaken in order to establish its tetrameric character and to ascertain the relationship of its structure to those of the stereochemically dissimilar $Co_4(CO)_{12}$ and $Ir_4(CO)_{12}$. Our interest in obtaining unambiguous molecular parameters for this complex in the *solid* state has been stimulated by recent work concerning the possible intramolecular rearrangement of $Co_4(CO)_{12}$ in solution.[7–9] All initial attempts to determine the crystalline structure of $Rh_4(CO)_{12}$ were unsuccessful owing to twinning and/or disorder of a different nature from that in the disordered crystalline structure of $Co_4(CO)_{12}$.[3a] Our continued effort to resolve this problem, however, has now provided the conclusive results reported here.

The rhodium tricarbonyl complex was synthesized by the high-pressure carbonylation of anhydrous $RhCl_3$

(1) Research jointly sponsored by the National Institutes of Health and the U. S. Atomic Energy Commission under contract with the Union Carbide Corporation, and by the National Science Foundation (GP 4919) at the University of Wisconsin.
(2) Presented in part by C. H. Wei at the National Meeting of the American Crystallographic Association, Minneapolis, Minn., Aug 20–25, 1967.
(3) (a) C. H. Wei and L. F. Dahl, *J. Am. Chem. Soc.*, 88, 1821 (1966); (b) P. Corradini, *J. Chem. Phys.*, 31, 1676 (1959); P. Corradini and A. Sirigu, *Ric. Sci.*, 36, 188 (1966).
(4) G. R. Wilkes, Ph.D. Thesis, University of Wisconsin, Madison, Wis., 1965; G. R. Wilkes and L. F. Dahl, to be published.
(5) W. Beck and K. Lottes, *Chem. Ber.*, 94, 2578 (1961).
(6) W. Hieber and H. Lagally, *Z. Anorg. Allgem. Chem.*, 251, 96 (1943).
(7) F. A. Cotton, *Inorg. Chem.*, 5, 1083 (1966).
(8) H. Haas and R. K. Sheline, *J. Inorg. Nucl. Chem.*, 29, 693 (1967).
(9) E. A. C. Lucken, K. Noack, and D. F. Williams, *J. Chem. Soc.*, Sect. A, 148 (1967).

with freshly reduced copper as halogen acceptor.[6] A large number of optically acceptable crystals, obtained by recrystallization from several organic solvents, were examined by X-ray diffraction photographs before crystallographically suitable crystals were found; these crystals invariably showed D_{2h}-mmm Laue symmetry. The resultant orthorhombic unit cell has lattice dimensions $a = 9.24$ A, $b = 12.02$ A, $c = 17.74$ A; $\rho_{obsd} = 2.58$ g cm^{-3} *vs.* $\rho_{calcd} = 2.52$ g cm^{-3} based on four $Rh_4(CO)_{12}$ species per cell. Systematic absences of l odd for $\{h0l\}$ and k odd for $\{0k0\}$ indicate a c glide and a 2_1 axis in the b direction.

Three-dimensional film data were collected with Mo Kα radiation from two tiny crystals from which 962 independent intensity maxima corresponding to one octant of the reflection sphere were obtained. Attempts to interpret a three-dimensional sharpened Patterson function in terms of any orthorhombic space group involving either or both of the above symmetry elements were unsuccessful. Instead the only trial model which conformed to the above symmetry and Patterson vector requirements (and which later was confirmed by least-squares refinement) was based on an incoherent twinning mechanism involving a monoclinic single crystal of symmetry P2$_1$/c and β angle of 90°. The presence of either a (100) or (001) twin mirror plane operating on the reciprocal lattice of this monoclinic unit cell would give rise to the same apparent unit cell for the twinned composite and thereby would result in the observed pseudo-orthorhombic diffraction symmetry with no streaking.[10,11]

The determination of the carbonyl positions in this twinned crystal was accomplished by successive Fourier syntheses for which application of derived mathematical relations[12] permitted a breakdown of the observed orthorhombic $|F(hkl)_o|^2$ data for the twinned composite into the $|F(hkl)_{o'}|$ and $|F(\bar{h}kl)_{o'}|$ coefficients for the monoclinic single crystal component. This Fourier analysis was complicated by the fact that the initial atomic coordinates obtained for the crystallographically

(10) Since completion of our structural analysis, we have learned from private correspondence (1967) that Dr. W. Murayama of the Central Laboratories of Ajinomoto Co., Inc. (Kawasaki, Japan), has also carried out an X-ray study of $Rh_4(CO)_{12}$. Although his attempts to unravel the carbonyl atomic positions from Fourier maps were unsuccessful, it is noteworthy that his interpretation of the orthorhombic crystal data was based on an identical monoclinic twinning model of symmetry P2$_1$/c.
(11) For either a (100) or (001) twinning plane the two enantiomorphous monoclinic reciprocal lattices (with $\beta^* = 90°$) superimpose so that the observed and calculated intensities, $|F(hkl)_o|^2$ and $|F(hkl)_c|^2$, for the pseudo-orthorhombic reciprocal lattice of the twinned composite are related to the corresponding quantities of the monoclinic reciprocal lattice, $|F(hkl)_{o'}|^2$ and $|F(\bar{h}kl)_{o'}|^2$ and $|F(hkl)_{c'}|^2$ and $|F(\bar{h}kl)_{c'}|^2$, by the following relationships

$$|F(hkl)_o|^2 = m|F(hkl)_{o'}|^2 + (1 - m)|F(\bar{h}kl)_{o'}|^2$$

$$|F(hkl)_c|^2 = m|F(hkl)_{c'}|^2 + (1 - m)|F(\bar{h}kl)_{c'}|^2$$

where m represents the fraction of one monoclinic component lattice. Since the symmetry of the twinned composite is orthorhombic within experimental error, m must be approximately 0.5. A value of $m = 0.504 \pm 0.009$ was obtained when m was refined as a variable parameter by least squares.
(12) In order to estimate magnitudes of the monoclinic structure factors, $F(\bar{h}kl)_{o'}$ and $F(\bar{h}kl)_{o'}$, the observed orthorhombic $|F(hkl)_o|^2$ was apportioned as follows.

$$|F(hkl)_{o'}| = \left[|F(hkl)_o|^2 \frac{|F(hkl)_{c'}|^2}{|F(hkl)_c|^2}\right]^{1/2}$$

$$|F(\bar{h}kl)_{o'}| = \left[|F(hkl)_o|^2 \frac{|F(\bar{h}kl)_{c'}|^2}{|F(hkl)_c|^2}\right]^{1/2}$$

independent tetrahedron of rhodium atoms were to a first approximation interrelated by a mirror plane coincident with the c_b glide plane in the centrosymmetic monoclinic unit cell. Because of this additional pseudo-mirror plane, the rhodium atoms made no contribution to the calculated structure factors for $\{hkl\}$ with l odd, and the generated space group $P2_1/m$ (obtained from a halving of the c-axis length through omission of the l odd reflections) was used for both the initial least-squares refinement[13,14] of the rhodium atoms and the subsequent Fourier synthesis phased on the rhodium atoms only. Hence, this first approximation to an electron-density map contained mirror-image peaks in addition to any peaks which possibly represented actual carbon and oxygen atoms. From stereochemical considerations supplemented by knowledge of the structure of $Co_4(CO)_{12}$, initial carbonyl position were obtained. Since the contribution of these light atoms to the calculated structure factors destroyed the quasi-mirror symmetry imposed by the rhodium atoms, all further Fourier maps and least-squares refinements[13,14] were based on the original monoclinic $P2_1/c$ space group with the inclusion of all diffraction data. These atom-seeking procedures were reiterated twice before all 24 light atoms were located. Final unweighted discrepancy values[15] based on isotropic full-matrix least-squares refinement[13,14] were $R_1(F)_T = 0.10$ and $R_1(F^2) = 0.17$.

In contrast to the disordered crystalline structure of $Co_4(CO)_{12}$ for which coherent scattering interference must occur, our crystalline samples of $Rh_4(CO)_{12}$ conform to an incoherent twinning model. However, the derived molecular structure of $Rh_4(CO)_{12}$ possesses a configuration strikingly similar to that of $Co_4(CO)_{12}$. Its idealized structure (Figure 1) of C_{3v}-3m symmetry consists of four tetrahedrally arranged rhodium atoms in which an apical $Rh(CO)_3$ group is symmetrically coordinated by only Rh–Rh bonds to a basal $Rh_3(CO)_9$ fragment containing three identical $Rh(CO)_2$ groups located at the vertices of an equilateral triangle and linked in pairs to one another by both a bridging carbonyl group and a Rh–Rh bond. The twelve CO groups are disposed at corners of an icosahedron which encompasses the tetrahedron of rhodium atoms. Of particular interest is the dissimilarity of this molecular structure with that of $Ir_4(CO)_{12}$ for which the idealized tetrahedral molecule of T_d-43m symmetry is stabilized by Ir–Ir bonds only (without bridging carbonyls).[4] This difference in structural type is the first proven case for corresponding metal carbonyls of the second- and third-row transition metal members of a group.

(13) The function minimized was $\Sigma w[|F(hkl)_o|^2 - s^2|F(hkl)_c|^2]^2$, where s is the adjusted scale factor.
(14) W. R. Busing, K. O. Martin, and H. A. Levy, "ORFLS, A Fortran Crystallographic Least-Squares Program," ORNL-TM-305, Oak Ridge National Laboratory, 1962.
(15) (a) For a twinned composite

$$R_1(F)_T = \frac{\Sigma\{||F(hkl)_{o'}| - s|F(hkl)_{c'}|| + ||F(\bar{h}kl)_{o'}| - s|F(\bar{h}kl)_{c'}||\}}{\Sigma\{|F(hkl)_{o'}| + |F(\bar{h}kl)_{o'}|\}}$$

(b)
$$R_1(F^2) = \frac{\Sigma||F(hkl)_o|^2 - s^2|F(hkl)_c|^2|}{\Sigma|F(hkl)_o|^2}$$

(c) For X-ray photographic data the usual unweighted $R_1(F)$ value for an untwinned crystal is normally about one-half the unweighted $R_1(F^2)$ [cf. G. M. Brown, Acta Cryst., 20, 921 (1966)]. The observed discrepancy factors are within an acceptable range for a successful structural determination and thereby signify that our incoherent twinning model must be essentially correct.
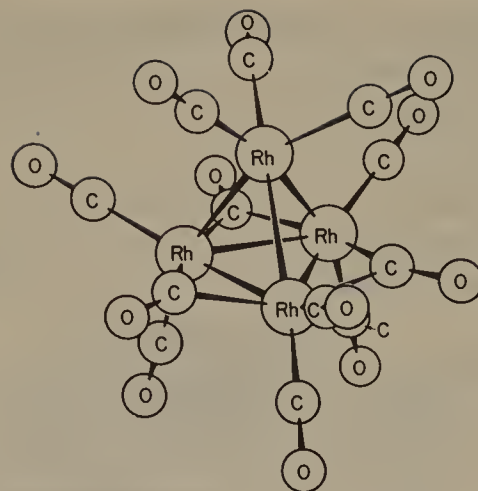
$Rh_4(CO)_{12}$

Figure 1. Molecular configuration of $Rh_4(CO)_{12}$.

The six Rh–Rh bonding distances in $Rh_4(CO)_{12}$ range from 2.70 to 2.80 A (individual esd, 0.01 A) with no apparent difference in length between the three carbonyl-bridged basal–basal Rh–Rh bonds and the three apical–basal Rh–Rh bonds. The weighted average Rh–Rh value of 2.73 A is 0.24 A longer then the average Co–Co bond length of 2.49 A (individual esd, 0.02 A) in $Co_4(CO)_{12}$ and 0.05 A longer than the average Ir–Ir bond length of 2.68 A (individual esd, 0.02 A) in $Ir_4(CO)_{12}$. It falls within the range of average Rh–Rh bond lengths observed in $[C_5H_5RhCO]_3$ (2.62 A),[16] $(C_5H_5)_2Rh_2(CO)_3$ (2.68 A),[16] rhodium metal (2.69 A),[17] and $Rh_6(CO)_{16}$ (2.78 A).[18] The average values for the other molecular parameters of $Rh_4(CO)_{12}$ are not unlike those in these other rhodium carbonyl complexes.

(16) O. S. Mills and E. F. Paulus, Chem. Commun., 815 (1966).
(17) Cf. L. E. Sutton, "Tables of Interatomic Distances and Configuration in Molecules and Ions," Special Publication No. 11, The Chemical Society, London, 1958, p S9.
(18) E. R. Corey, L. F. Dahl, and W. Beck, J. Am. Chem. Soc., 85, 1202 (1963).

Chin Hsuan Wei

Biology Division, Oak Ridge National Laboratory
Oak Ridge, Tennessee 37830

Glenn R. Wilkes, Lawrence F. Dahl

Department of Chemistry, University of Wisconsin
Madison, Wisconsin 53706

Received July 5, 1967

A Novel Isomerization in the Diels–Alder Reaction of α-Pyrone and Bis(trimethylsilyl)acetylene

Sir:

Derivatives of α-pyrone have been used to prepare aromatic compounds *via* Diels–Alder reactions with acetylenedicarboxylic acid esters,[1] and we have used the

(1) (a) K. Alder and H. F. Rickert, Ber., 70, 1354 (1937); (b) N. P. Shusherina, R. Ya. Levina, and V. M. Shostakovskii, Zh. Obshch. Khim., 29, 3237 (1959); (c) E. Wenkert, D. B. R. Johnston, and K. G. Dave, J. Org. Chem., 29, 2534 (1964).

Table I. Comparison of the Isomeric Bis(trimethylsilyl)benzenes with the Main Product of the α-Pyrone + $Me_3SiC{\equiv}CSiMe_3$ Reaction

Compound	Physical state	Glpc retention time,[a] min	$n^{25}D$
ortho isomer	Liquid	11.2	1.5108 (lit.[e] 1.5111)
meta isomer	Liquid	4.5	1.4852
para isomer	Solid, mp 95.4–95.5° (lit.[d] 92–93°)	6.5	(lit.[e] 1.4867)
Major product	Liquid	4.5	1.4870

|	Infrared spectrum,[b] cm^{-1}	Ultraviolet spectrum, mμ (ϵ)[c]
ortho	3120 (w), 3080 (m), 3050 (m), 2990 (sh, m), 2960 (s), 2905 (m), 1450 (w), 1412 (m), 1300 (w), 1265 (s), 1250 (s), 1167 (w), 1120 (s), 1055 (m), 1040 (m), 1005 (sh, w), 925 (sh, w), 840 (s), 755 (s), 740 (s), 698 (m), 690 (sh, m), 680 (sh, m), 655 (m)	λ_{sh} 222 (9330); λ_{sh} 258 (268); λ_{max} 264 (447); λ_{max} 270 (654); λ_{max} 277.5 (570)
meta	3070 (w), 3040 (w), 3020 (w), 2965 (s), 2900 (w), 1400 (w), 1365 (m), 1305 (w), 1260 (m), 1250 (s), 1175 (vw), 1150 (sh, w), 1140 (w), 1110 (m), 860 (s), 840 (s), 788 (w), 750 (s), 690 (m)	λ_{sh} 252 (113); λ_{max} 258 (189); λ_{max} 264 (276); λ_{max} 269 (266); λ_{max} 275 (179)
para	3050 (m), 2990 (sh, w), 2960 (s), 2895 (w), 1405 (w), 1375 (s), 1345 (w), 1325 (w), 1255 (sh, m), 1245 (s), 1185 (w), 1140 (s), 1130 (s), 1110 (sh, w), 845 (sh, s), 835 (s), 805 (s), 750 (s), 690 (m), 630 (m)	λ_{max} 225 (16,700); λ_{max} 229 (14,500); λ_{sh} 250 (147); λ_{max} 258 (264); λ_{max} 264 (390); λ_{max} 270 (405); λ_{max} 276 (322)
Major product	Identical with that of the *meta* isomer	λ_{sh} 252 (116); λ_{max} 258 (191); λ_{max} 264 (276); λ_{max} 269 (264); λ_{max} 275 (175)

[a] F & M Model 700, 12-ft 20% LAC-728 on Chromosorb W column at 120°, 60-cc/min helium flow. [b] Perkin-Elmer 237B. *ortho* and *meta* isomers determined as liquid films, *para* isomer in CCl_4 (4000–2000 cm^{-1}) and Nujol (2000–625 cm^{-1}). [c] Cary 14, in *n*-hexane solution. [d] A. D. Petrov, E. A. Chernyshev, and L. Guan-lian, *Dokl. Akad. Nauk SSSR*, **132**, 1099 (1960). [e] Reference 5.

reaction of this diene with bis(trimethyltin)acetylene to prepare o-bis(trimethyltin)benzene.[2] In these examples the acetylene substituents occupied vicinal positions in the resulting benzene derivative, as might be expected in a process in which loss of carbon dioxide from the initial adduct and aromatization occur in a concerted fashion (eq 1). In view of this simple picture, the results presented in this communication are rather unexpected.

(1)
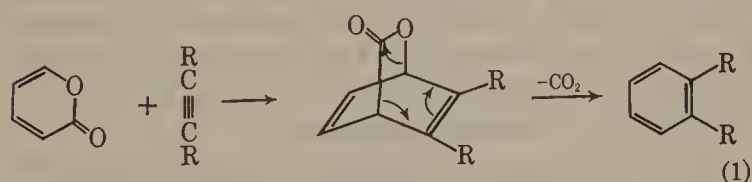
A solution of α-pyrone (11 mmoles) and bis(trimethylsilyl)acetylene (14.8 mmoles) in 2 ml of bromobenzene was heated at reflux (135–145°) under argon for 4.5 days. Distillation of the reaction mixture gave 1.3 g (53%) of liquid, bp 32° (0.1 mm), which glpc analysis showed to contain one major component in addition to trace quantities of three others. The major component gave the correct analysis for $C_{12}H_{22}Si_2$, but it was m-bis(trimethylsilyl)benzene rather than the expected *ortho* isomer (eq 2). Identification of the major product as the *meta* isomer is based upon comparison of its glpc retention time, refractive index, and infrared, nmr, and ultraviolet spectra with those of authentic samples of the three isomeric bis(trimethylsilyl)benzenes. These, all known compounds,[3] were prepared by the Barbier procedure.[4] Pertinent data are given in Table I. The minor products, presumed to be the *ortho* and

(2) A. B. Evnin and D. Seyferth, *J. Am. Chem. Soc.*, 89, 952 (1967).
(3) H. A. Clark, A. F. Gordon, C. W. Young, and M. J. Hunter, *ibid.*, 73, 3798 (1951).
(4) R. G. Chaffee and H. N. Beck, *J. Chem. Eng. Data*, 8, 453, 602 (1963).

meta isomers, were present in too small a quantity to permit their isolation, and their identification is based on glpc retention time only. It is important to note that the *ortho* isomer is thermally stable under the reaction conditions and does not undergo rearrangement to the *meta* isomer.

(2)
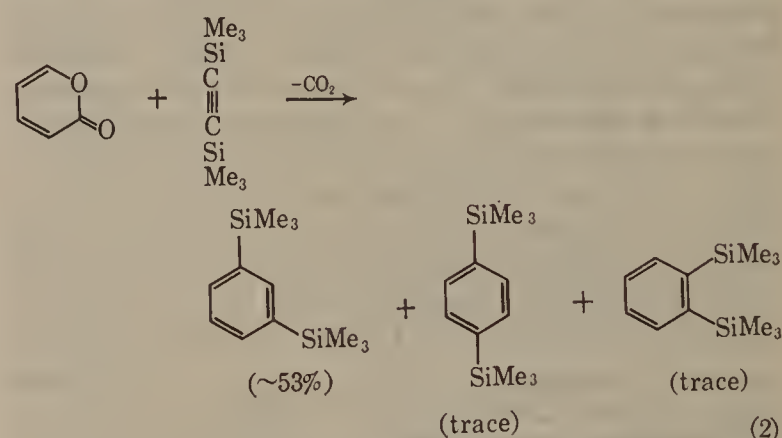
We suggest that the formation of m-bis(trimethylsilyl)benzene in this reaction is a consequence of the steric strain associated with the two vicinal, highly branched trimethylsilyl groups attached to sp^2 carbon atoms. At least three routes which lead ultimately to the observed product may be envisaged: (1) extrusion of carbon dioxide from the initial adduct I with formation of prismane II which then isomerizes to m-bis(trimethylsilyl)benzene; (2) extrusion of carbon dioxide from I with formation of the benzvalene III, isomerization of which would give the observed product; (3) extrusion of carbon dioxide from I with formation of o-bis(trimethylsilyl)benzene in a vibrationally excited ground state, followed by isomerization of the latter to the *meta* isomer *via* II and/or III. These routes are illustrated in Chart I. A diradical intermediate, IV,

possibly could be involved in the formation of II and III. Since this reaction was carried out in solution,

IV
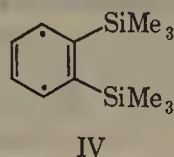
route 3 seems the least likely. However, route 3 is a formal analog of Burgstahler's photoisomerization of o-di-t-butylbenzene to a mixture of the *meta* and *para* isomers,[5] for which a prismane,[5] interconvertible Dewar structures,[6] and a benzvalene[6] have been suggested as intermediates. This analogy suggested that one might observe similar isomerization of o-bis(trimethylsilyl)-benzene upon irradiation. Such was the case: when 3.43 mmoles of this compound in 50 ml of diethyl ether was irradiated in a Rayonet photochemical reactor, a 12.4:1 mixture of o- and m-bis(trimethylsilyl)-benzene, as well as a trace amount of the *para* isomer, was present after a 24-hr reaction time. That such isomerization did occur (presumably *via* II and/or III) suggests that the paths we list above for the thermal Diels–Alder reaction are possible and even plausible routes to the observed *meta* isomer.

Chart I
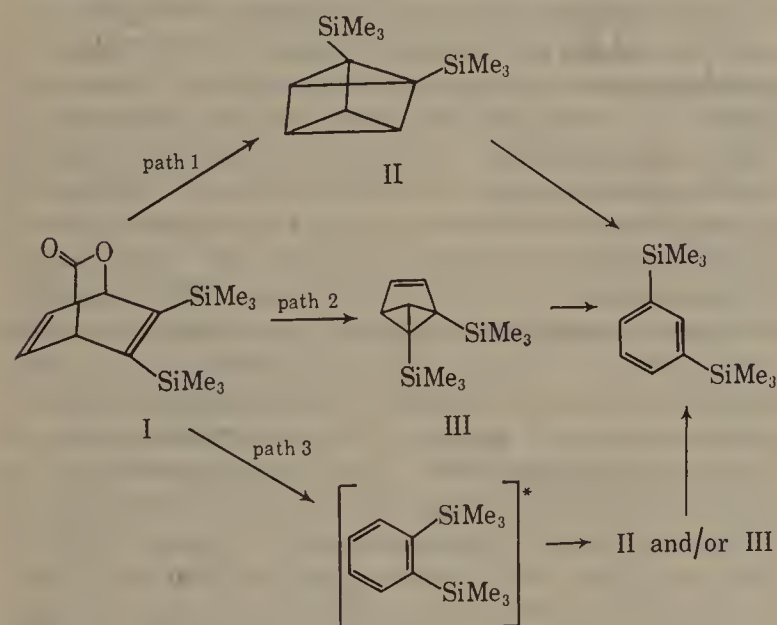
There remains the problem of why α-pyrone and Me₃SnC≡CSnMe₃ react to give o-bis(trimethyltin)-benzene, while in the corresponding reaction of Me₃SiC≡CSiMe₃ the *meta* isomer is produced. In this connection it is noteworthy that attempts to photo-isomerize o-bis(trimethyltin)benzene thus far have been unsuccessful. Perhaps then the excited state of this molecule is less sterically strained than is that of its silicon analog, and this in turn may have some implications with respect to the thermal Diels–Alder reaction of bis(trimethyltin)acetylene and its silicon analog with α-pyrone. In general, steric effects associated with Me₃M^{IV} groups decrease with increasing size of M^{IV}: C > Si > Ge > Sn. However, other factors may be of importance in the excitation of these ortho-disubstituted benzenes.

(5) (a) A. Burgstahler and P.-L. Chien, J. Am. Chem. Soc., 86, 2940 (1964); (b) A. Burgstahler, P.-L. Chien, and M. O. Abdel-Rahman, ibid., 86, 5281 (1964).
(6) L. Kaplan, K. E. Wilzbach, W. G. Brown, and S. S. Yang, ibid., 87, 675 (1965).

Further studies of α-pyrones and 5,5-dimethoxytetrachlorocyclopentadiene[7] with Me₃M^{IV}C≡CM^{IV}Me₃ compounds (M^{IV} = C, Si, Ge, Sn, Pb) are being carried out with the aim of determining which factors are of importance with respect to the question of isomerization *vs.* absence of isomerization in these Diels–Alder reactions, as are more detailed investigations of o-(Me₃-M^{IV})₂C₆H₄ compounds and their photochemical transformations.

(7) Note the reaction of this compound with bis(trimethyltin)acetylene, which gives 1,2-bis(trimethyltin)tetrachlorobenzene: D. Seyferth and A. B. Evnin, ibid., 89, 1468 (1967).
(8) National Institutes of Health Predoctoral Fellow, 1963–1966.

Dietmar Seyferth, David R. Blank, Anthony B. Evnin[8]
Department of Chemistry, Massachusetts Institute of Technology
Cambridge, Massachusetts 02139
Received June 14, 1967

On the Mechanism of the Photochemical Decomposition of Cyclobutanone in the Gas Phase[1]

Sir:

The photochemical decomposition of cyclobutanone in the gas phase yields ethylene and ketene or cyclopropane, propylene, and CO,[2,3] and only a negligible amount of the expected rearrangement product (3-butenal?) has been detected.[4,5] Recently a pressure-dependence study of the ratio of propylene to cyclopropane led to the conclusion that propylene is a secondary product arising from the unimolecular decomposition of an excited cyclopropane,[6,7a] and a theoretical model for internal energy distribution in the photochemical excitation and the unimolecular decomposition processes has been developed.[7b] As far as the photochemical intermediate responsible for the observed decomposition products is concerned, it has been suggested to be an acyl diradical of the type ĊH₂–CH₂–CH₂–ĊO.[2,3,8]

We have shown that the benzene-photosensitization technique[9,10] can be very useful for a mechanistic diagnosis of the gas-phase photochemical reactions of 4-pentenal[11] and cyclopentanone.[12] The singlet–singlet

(1) This research has been supported by a National Science Foundation grant (GP 6924).
(2) S. W. Benson and G. B. Kistiakowsky, J. Am. Chem. Soc., 64, 80 (1942).
(3) F. E. Blacet and A. Miller, ibid., 79, 4327 (1957).
(4) R. Srinivasan, ibid., 81, 5541 (1959).
(5) See, for a review of the photochemistry of cyclic ketones, R. Srinivasan, Advan. Photochem., 1, 84 (1963).
(6) R. G. Klemm, D. N. Morrison, P. Gilderson, and A. T. Blades, Can. J. Chem., 43, 1934 (1965).
(7) (a) R. J. Campbell, E. W. Schlag, and B. W. Ristow; (b) R. J. Campbell and E. W. Schlag, private communication, to be published.
(8) M. C. Flowers and H. M. Frey, J. Chem. Soc., 2758 (1960). The trimethylene diradical, an assumed decomposition product of this acyl diradical intermediate, has been reported to react with excess ethylene to yield C₅ olefins as trapped products, but attempts to confirm this result have so far failed (see ref 6 and 7a).
(9) (a) H. Ishikawa and W. A. Noyes, Jr., J. Am. Chem. Soc., 84, 1502 (1962); J. Chem. Phys., 37, 583 (1962); (b) W. A. Noyes, Jr., and I. Unger, Advan. Photochem., 4, 49 (1966).
(10) R. B. Cundall, F. J. Fletcher, and D. G. Milne, Trans. Faraday Soc., 60, 1146 (1964).
(11) E. K. C. Lee and N. E. Lee, J. Phys. Chem., 71, 1167 (1967).
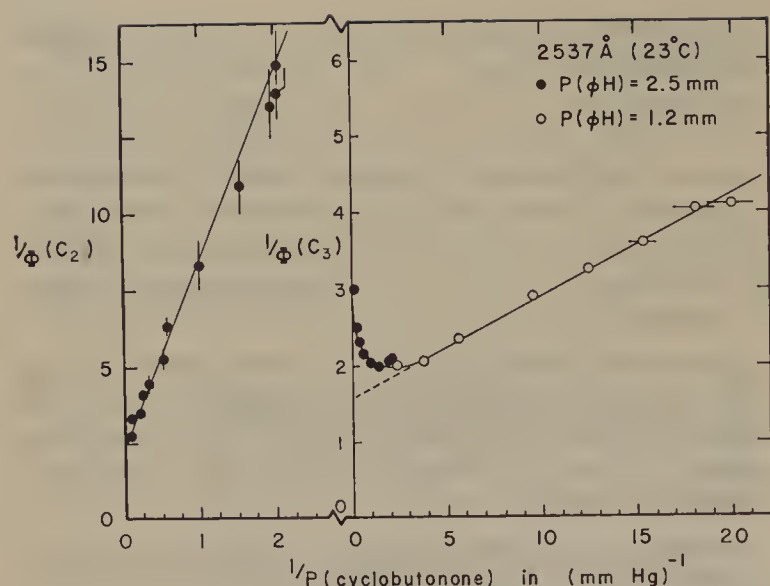(12) E. K. C. Lee, ibid., 71, 2804 (1967).

Figure 1. The inverse pressure dependence of the inverse quantum yields: left, the singlet sensitization; right, the triplet sensitization.

energy transfer predominates at relatively high acceptor pressures while the triplet–triplet energy transfer predominates at lower pressures since the $^1B_{2u}$ state benzene intersystem-crosses to the $^3B_{1u}$ state.[9-14] Now we wish to report the results of the benzene photosensitized decomposition and direct photochemical decomposition of cyclobutanone in the gas phase and to present a mechanistic and energetic interpretation of the decompositions of excited cyclobutanones.

The experimental procedures and the kinetic treatment used in this work are described elsewhere in detail.[11,12] The most significant finding from this work is that two distinct primary photochemical processes in the direct photolysis of cyclobutanone can be explained as follows: (1) the decomposition of the excited singlet cyclobutanone to give ethylene and ketene, and (2) the intersystem crossing of the excited singlet cyclobutanone to its low-lying triplet state from which an excited cyclopropane and CO result by the subsequent decomposition. This mechanistic interpretation is based on the data present in Figure 1, in which the inverse sensitization quantum yields of ethylene (C_2) and of cyclopropane plus propylene (C_3) are plotted against the inverse cyclobutanone pressure.

From this Stern–Volmer type plot, then, a limiting value for the sensitized quantum yield of ethylene is found to be ∼0.5 by extrapolation to the infinite cyclobutanone pressure. The quantum yield of ethylene is one-half of this limiting value at 3.0 mm of cyclobutanone pressure. This and our other observation that 50% of the fluorescence emission by the $^1B_{2u}$ benzene is quenched by 3.0 mm of cyclobutanone provide sufficient evidence for a singlet–singlet energy-transfer process in which an excited singlet cyclobutanone is formed with an effective cross section of ∼1.3 A². The subsequent decomposition of the excited singlet cyclobutanone yields ethylene and ketene as characteristic singlet decomposition products.

The yield of the C_3 hydrocarbons is monotonically decreased by an increasing amount of cis-2-butene, and this implies that these products are characteristic decomposition products of the excited triplet cyclobutanone, since cis-2-butene is capable of quenching the long-lived triplet benzene intermediate.[9,10] Our measurements show that cyclobutanone is only one-fourth as effective as cis-2-butene in competing for the triplet benzene sensitization. The deviation of the triplet sensitization quantum yield from the straight-line behavior of the Stern–Volmer type plot at high cyclobutanone pressures in Figure 1 is expected, since the diminution of the intersystem crossing of the $^1B_{2u}$ benzene due to more efficient singlet–singlet energy transfer at this pressure lowers the $^3B_{1u}$ benzene population.[12] The limiting value of the triplet quantum yield is ∼0.7, which is the maximum value expected in the triplet benzene sensitization,[10] and the half-pressure for this sensitization is 0.10 mm of cyclobutanone. It has been shown previously that the ratio of propylene to cyclopropane is a measure of internal energy of the excited cyclobutanone.[6,7] The observed ratio of propylene to cyclopropane in triplet benzene photosensitization indicates that, on the average, 80–85 kcal/mole of excitation energy is transferred to cyclobutanone from the triplet benzene, as compared to about 99 kcal/mole in the singlet benzene photosensitization of cyclopentanone.[12]

In view of the fact that the thermal decomposition of cyclobutanone in gas phase yields mainly ethylene and ketene,[15] it is not so surprising to find these as decomposition products of the photochemically excited singlet cyclobutanone. However, it is very interesting to note that cyclopropane with a substantial quantum yield in the direct photolysis (0.14 at 3130 A and 0.29 at 2654 A where $t = 100-300°$ and $p = 100-150$ mm)[3] presumably arises from the triplet cyclobutanone decomposition. The ratio of the C_3 yield to the C_2 yield in direct photolysis is indicative of the extent of the intersystem crossing of the excited singlet cyclobutanone to the low-lying triplet state. Our measurements of this ratio at various excitation wavelengths at about 10-mm pressure of cyclobutanone and at 23° are as follows: 0.41 ± 0.02 at 3200 A, 0.64 ± 0.03 at 2800 A, 0.79 ± 0.04 at 2537 A, and 0.93 ± 0.04 at 2480 A. A comparable experimental set of data such as these has been obtained in another laboratory.[7] These results then strongly suggest that the intersystem crossing of the excited singlet cyclobutanone increases with increasing photoexcitation energy and that it plays a very important role in direct photolysis of cyclobutanone. A similar interpretation can also be given for the intersystem crossing of the $^1B_{2u}$ benzene.[16,17] Both examples are worthy of further study. Recent studies of the trimethylene diradical produced by the addition of the triplet methylene to ethylene show that the trimethylene diradical ring-closes to cyclopropane if collisionally deexcited,[18,19] and this analogy favors a mechanism for the formation of cyclopropane via a triplet

(13) J. W. Donovan and A. B. F. Duncan, J. Chem. Phys., 35, 1389 (1961). The lifetime of the $^1B_{2u}$ benzene has been measured to be ∼0.6 μsec.

(14) C. S. Parmenter and B. L. Ring, ibid., 46, 1998 (1967). The lifetime of the $^3B_{1u}$ benzene at 20-mm benzene pressure has been measured to be ∼26 μsec.

(15) M. N. Das, F. Kern, T. D. Coyle, and W. D. Walters, J. Am. Chem. Soc., 76, 6271 (1954).

(16) G. B. Kistiakowsky and C. S. Parmenter, J. Chem. Phys., 42, 2942 (1965).

(17) S. Strickler and R. J. Watts, ibid., 44, 426 (1966).

(18) C. McKnight, E. K. C. Lee, and F. S. Rowland, J. Am. Chem. Soc., 89, 469 (1967).

(19) R. J. Cvetanović, H. E. Avery, and R. S. Irwin, J. Chem. Phys., 46, 1993 (1967).

acyl diradical in the photochemical decomposition of cyclobutanone in the gas phase. Further investigation in this direction will be reported in more detail.

H. O. Denschlag, Edward K. C. Lee
*Department of Chemistry, University of California
Irvine, California 92664*
Received June 28, 1967

The Structure and Configuration of "Neutral Plasmalogens" [1]

Sir:

Previous reports suggested the occurrence of minute amounts of aldehydogenic neutral lipids in various mammalian tissues.[2] Small quantities of "neutral plasmalogens" have also been found in man.[3]

We have detected neutral plasmalogens in flesh, liver, and eggs of the shark *Hydrolagus colliei* ("ratfish") and have separated them by adsorption chromatography from the major lipid constituents of these tissues, *viz.*, O-alkyldiglycerides and triglycerides.[4] The total lipids of ratfish liver contained about 5% of neutral plasmalogens and thus constituted a convenient source. A pure fraction (**1**) was obtained by repeated chromatography of ratfish liver lipids on layers of silicic acid.[5] Fraction **1** yielded O-alkyldiglycerides (**2**) upon catalytic hydrogenation. Treatment with hydrochloric acid[4] did not affect **2**, whereas **1** yielded a mixture of aldehydes and diglycerides. Reaction of **2** with methanolic hydrogen chloride at 80° yielded alkyl glycerol ethers and methyl esters of fatty acids; **1** afforded dimethyl acetals of aldehydes and methyl esters. Upon reaction with lithium aluminum hydride in diethyl ether and subsequent acid-catalyzed hydrolysis, **2** afforded alkyl glycerol ethers and alcohols, **1** afforded aldehydes and alcohols. In contrast, decomposition of the lithium alumino complex obtained from **1**, by water, gave alcohols and alk-1-enyl glycerol ethers. The latter compounds migrated on adsorbent layers slightly ahead of alkyl glycerol ethers and could be cleaved to aldehydes and glycerol by acid-catalyzed hydrolysis.

These findings indicated that the fraction (**1**) isolated from ratfish liver lipids consisted of O-alk-1-enyldiglycerides. The quantity we have prepared was sufficient to determine the position of the alk-1-enyloxy group, the optical configuration of the glycerol moiety, and the geometric configuration of the enolic double bond.

Figure 1.

The alkyl glycerol ethers derived from **1** could be cleaved with sodium metaperiodate and formed isopropylidene ketals with acetone. These reactions and the optical activity of both **1** and **2** proved that these compounds were derivatives of alkyl 1-glycerol ethers, *i.e.*, the asymmetrical isomers. The specific optical rotation[6] of **1** was $[\alpha]^{25}$D +2.0° (*c* 1.9); that of **2** was $[\alpha]^{25}$D −2.8° (*c* 1.8), which is in numerical agreement with the specific optical rotation found for a synthetic L-alkyldiglyceride[7] ($[\alpha]^{25}$D +4.0° (*c* 2.6)). Thus, **1** can be assigned to the D series to which all naturally occurring alkyl 1-glycerol ethers belong.[8,9]

The infrared absorption spectrum[10] of **1** is rather similar to that of **2** and to a synthetic O-alkyldiglyceride.[7] Additional bands associated with the enol ether grouping are those near 1668–1666 and 732–730 cm⁻¹, which are due to a stretching vibration of the carbon double bond in the position α to the ether linkage and to a C–H out-of-plane deformation of the same group, respectively. Both bands were found also in spectra of naturally occurring alk-1-enyl acyl glycerophosphatides and were shown to be strictly associated with the *cis*-alk-1-enyl ether linkage, whereas the spectra of *trans*-alk-1-enyl ethers are known to exhibit doublets near 1670 cm⁻¹ and a band near 930 cm⁻¹.[11,12]

The nuclear magnetic resonance spectrum[13] of **1** (see Figure 1) shows a doublet centered at δ 5.89 ppm which accounts for the olefinic hydrogen at the carbon in the position α to the ether linkage. This doublet is associated with the hydrogen at the *cis* enol ether bond, whereas the *trans* isomer would show a doublet near 6.20 ppm (and a pair of triplets near 4.78 ppm).[12] The signal of the olefinic hydrogen at C-2′ near 4.5 ppm is partially embedded in the multiplet centered at 4.30

(1) This investigation was supported in part by Public Health Service Research Grants GM 05817 and HE 08214 from the National Institutes of Health.
(2) M. L. Karnovsky, S. S. Jeffrey, M. S. Thompson, and H. W. Deane, *Biophys. Biochim. Cytol.*, 1, 173 (1955); J. Eichberg, J. R. Gilbertson, and M. L. Karnovsky, *J. Biol. Chem.*, 236, PC15 (1961); J. C. M. Schogt, P. H. Begemann, and J. Koster, *J. Lipid Res.*, 1, 446 (1960); J. R. Gilbertson and M. L. Karnovsky, *J. Biol. Chem.*, 238, 893 (1963).
(3) H. H. O. Schmid, N. Tuna, and H. K. Mangold, *Z. Physiol. Chem.*, 348, 730 (1967).
(4) H. H. O. Schmid and H. K. Mangold, *Biochim. Biophys. Acta*, 125, 182 (1966).
(5) Plates coated with layers of silica gel H (Merck), 2 and 0.5 mm thick, were developed twice with hexane–diethyl ether (95:5, v/v). Diethyl ether was used to elute the material from the adsorbent.
(6) Optical rotations were measured at 25° with a Bellingham and Stanley polarimeter, using chloroform as solvent.
(7) W. J. Baumann and H. K. Mangold, *J. Org. Chem.*, 29, 3055 (1964); W. J. Baumann and H. K. Mangold, *Biochim. Biophys. Acta*, 116, 570 (1966).
(8) E. Baer and H. O. L. Fischer, *J. Biol. Chem.*, 140, 397 (1941).
(9) Alk-1-enyl acyl glycerophosphatides ("plasmalogens") recently were shown to possess the D configuration as well: J. C. Craig, D. P. G. Hamon, K. K. Purushothaman, S. K. Roy, and W. E. M. Lands, *Tetrahedron*, 22, 175 (1966).
(10) Infrared spectra were recorded with a Perkin-Elmer Model 21 spectrophotometer. Carbon disulfide served as solvent, except in the ranges 2400–2000 and 1650–1400 cm⁻¹, where tetrachloroethylene was used.
(11) W. T. Norton, E. L. Gottfried, and M. M. Rapport, *J. Lipid Res.*, 3, 456 (1962); H. R. Warner and W. E. M. Lands, *J. Am. Chem. Soc.*, 85, 60 (1963).
(12) J. C. Craig and D. P. G. Hamon, *J. Org. Chem.*, 30, 4168 (1965).
(13) Nuclear magnetic resonance spectra were taken in CDCl₃ with tetramethylsilane as the internal standard using a Varian A-60A spectrometer.

ppm which is considered to be characteristic of the acylated H_2CO group of glycerol.[14] Additional signals are: a triplet at 0.89 ppm, accounting for the terminal methyl groups; a single peak at 1.28 ppm, associated with the internal methylene groups of the aliphatic chains; a triplet at 5.37 ppm, representing the isolated olefinic groups; and an apparent doublet corresponding to the CH_2 groups in the position α to the carbon double bonds centered at 2.03 ppm. The doublet which appears at 2.27 ppm can be correlated with an α-CH_2 group of the acyl functions. The apparent doublet occurring at 3.83 ppm can be assigned to the CH_2O group of glycerol connected to the ether linkage. The signal of the acylated HCO group of glycerol near 5.17 ppm is partially obscured by the triplet representing the isolated carbon double bonds. A signal near 2.9 ppm, characteristic of a methylene group between two double bonds,[14] is absent. Approximately two out of three aliphatic chains per molecule are monounsaturated.

$$
\begin{array}{c}
\text{O} \\
\parallel \\
H_2C-O-C-R'' \\
\mid \qquad \text{O} \\
\mid \qquad \parallel \\
H-C^*-O-C-R' \\
\mid \\
H_2C-O \\
\end{array}
$$
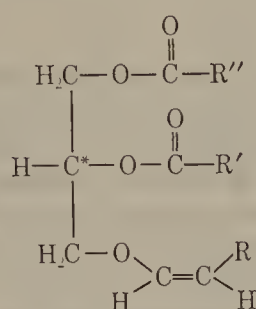
Chemical reactions, specific optical rotations, and spectroscopic data prove that the fraction (1) isolated from the liver of *Hydrolagus colliei* consisted of D(+)-1-O-*cis*-alk-1'-enyldiglycerides.

(14) C. Y. Hopkins in "Progress in the Chemistry of Fats and Other Lipids," Vol. 8, R. T. Holman, Ed., Pergamon Press, New York, N. Y., p 213.

H. H. O. Schmid, W. J. Baumann, H. K. Mangold
University of Minnesota, The Hormel Institute
Austin, Minnesota 55912

Oligodeoxynucleotide–Polydeoxynucleotide Interactions. Adenine–Thymine Base Pairs[1]

Sir:

Quantitative data on the interaction of structurally defined oligonucleotides with complementary polynucleotides are of value in practical and theoretical studies on nucleic acid structure. An investigation of oligodeoxynucleotide–polydeoxynucleotide interactions, covering a broad range of chain lengths in both members of the interacting pairs, displays partial confirmation of theory and some anomalous behavior.

A series of oligodeoxynucleotides, $d(pA)_m$ and $d(pT)_m$[2] with $m = 2$–25, was prepared by DNase I degradation of $d(pA)_n$ and $d(pT)_n$ followed by chromatog-

(1) Supported by Grant CA-08487 from the U. S. Public Health Service.

(2) Abbreviations used: m, oligonucleotide chain length; n, a polymer chain length greater than 300 nucleotides; $T_{1/2}$, temperature at the midpoint of the ultraviolet thermal transition in degrees Kelvin; $d(pA)_m$ and $d(pT)_m$, deoxyadenylate and deoxythymidylate oligonucleotides bearing a 5'-phosphate group and a 3'-hydroxyl group; $d(pA)_n$, polydeoxyadenylate; $d(pT)_n$, polydeoxythymidylate; DNase I, pancreatic deoxyribonuclease; ribonucleotide polymers are prefixed by r.

raphy on diethylaminoethylcellulose.[3] The melting behavior of the complexes $d(pA)_m + d(pT)_n$, $d(pA)_n + d(pT)_m$, and $d(pA)_n + d(pT)_n$, formed by mixing the constituents in a suitable solvent, was then observed by ultraviolet absorbance changes. The stoichiometry of the interactions was determined from mixing curves or (more directly) by gel filtration on Sephadex G-200.[4]

The interaction of $d(pA)_n$ with $d(pT)_m$ follows the relationship $1000/T_{1/2} = A + B/m$ and the stoichiometry is 1:1 in equimolar mixtures in all solvents used (Table I). This interaction is a multimolecular process

Solvent	Oligo-P concn, $M \times 10^6$	A	B
NaCl, 0.15 M; sodium citrate, 0.015 M (SSC)	14.0	2.88	4.57
	55.0	2.88	4.13
Potassium phosphate, 40 mM, pH 7	13.5	2.97	4.78
Potassium phosphate, 40 mM, pH 7, with 8 mM MgCl$_2$	14.5	2.88	4.26

[a] The relationship, $1000 T_{1/2} = A + B/m$ is observed. The values in the table are A and B for this equation, in different solvents and at different oligodeoxynucleotide concentrations (expressed in nucleotide residues). Polymer is present in an equivalent amount.

and thus $T_{1/2}$ values[5] (Table I) and the slope of the transition are quite sensitive to oligonucleotide concentration. These results are in accord with statistical thermodynamic treatment of oligo and polymer interactions.[6]

The interaction of equimolar amounts of $d(pA)_m$ with $d(pT)_n$ in SSC is complicated by a change in the stoichiometry of the *major* complex present to 1A–2T when $m < 16$. The double-stranded (1:1) complex is not detected in the interaction involving $d(pA)_7$, but it is clearly evident as an early rise in absorbance at 260 mμ (or a decrease at 284 mμ) when $d(pA)_m$, $m = 8$–12, complexes with $d(pT)_n$ are melted. The presence of complexes of different stoichiometry in the mixture could result from a slow approach to equilibrium. Repeated analysis on an equimolar mixture of $d(pA)_8$ and $d(pT)_n$ over a period of 3 months demonstrated that the amounts of double helix and triple helix, detected by melting, remain unchanged. We conclude that an equilibrium mixture of double and triple helices are present in this case. The triple-stranded complexes $d(pA)_m$–$2d(pT)_n$ (with $m < 16$), obtained by mixing the

(3) F. J. Bollum, "Procedures in Nucleic Acid Research," G. Cantoni and D. Davies, Ed., Harper and Row, Inc., New York, N. Y., 1966, pp 577–592.

(4) Separations were made on a 1 × 100 cm column on Sephadex G-200 equilibrated with the appropriate solvent and developed at a temperature about 15° below the $T_{1/2}$ of the complex to be tested. Detailed results will be presented in a future publication.

(5) M. N. Lippsett, L. A. Heppel, and D. F. Bradley, *Biochim. Biophys. Acta* 41, 175 (1960), have observed the dependence upon the total nucleotide concentration in a study of the interactions of r(pA)$_m$ with poly rU.

(6) (a) W. S. Magee, Jr., J. H. Gibbs, and B. H. Zimm, *Biopolymers*, 1, 133 (1963). Note that the authors have called attention to the dependence on absolute activity of the oligonucleotide in eq 19, and in accordance with their treatment our $B = B'$ ln CD, where B' = slope at unit activity, C = absolute activity of the m-mer, and D = the ratio of two internal partition functions. We assume that the absolute activity is essentially constant for all m-mers at the nucleotide residue concentration used (15 × 10⁻⁶ M). (b) W. S. Magee, Jr., J. H. Gibbs, and G. F. Newell, *J. Chem. Phys.*, 43, 2115 (1965).

constituents in 1:2 proportion, undergo a single-step thermal transition observed at 260 and 284 mμ. The latter wavelength is specific for the triple strand melting.[7] Values of $1/T_{1/2}$, when $m = 6$–9, for an oligonucleotide residue concentration of 10 μM do follow a linear relationship, but $A = 3.05$ and $B = 2.20$ (Figure 1). The 1:1 complex for equimolar mixtures of d(pA)$_m$ and d(pT)$_n$ is completely formed only when $m > 16$ in SSC, and these double-stranded complexes have $T_{1/2}$ similar (within the range of our experimental error, $\pm 0.5°$) to those formed by d(pA)$_n$ and d(pT)$_m$ at equal values of m.[8] $1/T_{1/2}$ values now fit on the same line (Figure 1). The anomalous stoichiometry described above for a Na$^+$ concentration of 0.19 M (SSC) is also exhibited in 40 mM phosphate buffer, pH 7.0, with or without the presence of 8 mM MgCl$_2$ (data not presented here).[9]

The over-all reactions that may be postulated to occur in our studies are given in eq 1–3 (major complex at equilibrium is underlined) when equimolar amounts of

$$\text{d(pA)}_n + \text{d(pT)}_n \underset{}{\overset{}{\rightleftarrows}} \underline{\text{d(pA)}_n\text{–d(pT)}_n} \overset{}{\rightleftarrows}$$
$$\underline{\text{d(pA)}_n\text{–2d(pT)}_n} + \text{d(pA)}_n \quad (1)$$

$$\text{d(pA)}_n + \text{d(pT)}_m \underset{}{\overset{}{\rightleftarrows}} \underline{\text{d(pA)}_n\text{–d(pT)}_m} \overset{}{\rightleftarrows}$$
$$\underline{\text{d(pA)}_n\text{–2d(pT)}_m} + \text{d(pA)}_n \quad (2)$$

$$\text{d(pA)}_m + \text{d(pT)}_n \overset{}{\rightleftarrows} \underline{\text{d(pA)}_m\text{–d(pT)}_n} \overset{}{\rightleftarrows}$$
$$\underline{\text{d(pA)}_m\text{–2d(pT)}_n} + \text{d(pA)}_m \quad (3)$$
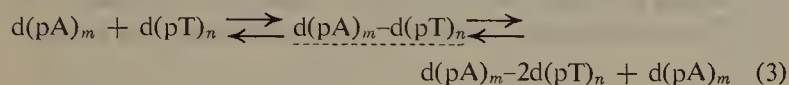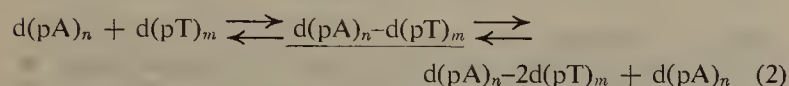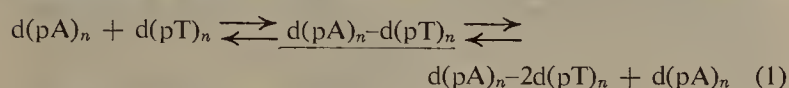
reactant residues are mixed. Reaction 1 is analogous to the interaction of rA with rU because stable 1:1 and 1:2 complexes are formed at equilibrium when the two polymers are mixed in the 1:1 and 1:2 proportion. The kinetics of the approach to the equilibrium in the equimolar mixture of the two polymers are also similar because the complex d(pA)$_n$–2d(pT)$_n$, detected by differential spectroscopy at 284 mμ, is a transient form as in the case of rA–rU formation.[10] In reaction 2 the triple-stranded complex is not formed in equimolar mixture at $m < 11$ (probably because the conditions are not permissive), and we find that equilibrium is reached a few seconds after mixing. We anticipate that as m increases 1A–2T complexes will be observed in 1:1 and 1:2 mixtures. In reaction 3 we notice that the ability of d(pA)$_m$ to compete with d(pT)$_n$ held in the three-stranded configuration increases with increasing value of m. The equilibrium point for this reaction at $m < 16$ (SSC) is shifted toward the triple-stranded helix.

All of this discussion can be summed up by noting that an extrapolation of the $T_{1/2}$ line for triple-stranded complex to the $T_{1/2}$ axis would cross the line for two-stranded complexes (Figure 1). This means that there will be a region of m where three-stranded complexes are more stable than two-stranded complexes. The melting transitions here will be three → one. There is also a region where three-stranded complexes are less

(7) M. Riley, B. Maling, and M. J. Chamberlin, *J. Mol. Biol.*, **20**, 359 (1966); F. J. Bollum, unpublished data, 1965.

(8) A. M. Michelson, *Boll. Soc. Chem. Biol.*, **47**, 1553 (1965), has shown that complexes of different stability are formed when r(A)$_m$ or r(U)$_m$ of the same chain length are mixed with the complementary ribopolymer, but the stoichiometry of the complexes formed was not discussed.

(9) The choice of solvents may be considered arbitrary, but in fact the Mg^{2+} phosphate buffer is used for the enzymatic replication of homopolydeoxynucleotides. This investigation was a result of problems encountered in the replication study.

(10) R. D. Blake and J. R. Fresco, *J. Mol. Biol.*, **19**, 145 (1966).

Figure 1. Melting temperature *vs.* chain length for oligodeoxynucleotide–polydeoxynucleotide complexes. Plot of the reciprocal midpoint of the thermal transition (in degrees Kelvin) of complexes formed by mixing oligodeoxynucleotides with complementary deoxypolymers as a function of the reciprocal chain length of the oligodeoxynucleotide. The total nucleotide residue concentration of the mixtures was 30 μM. The line was determined by least squares: ●, d(pA)$_n$–d(pT)$_m$ mixtures; △, d(pA)$_m$–d(pT)$_n$ mixtures; ■, d(pA)$_n$–d(pT)$_n$ mixture.

stable than two-stranded complexes. Here melting transitions will be three → two → one.

The value of m at the cross point is also related to the solvent used. We anticipate that there should be a low salt concentration where all d(pA)$_m$ form a double-stranded complex with d(pT)$_n$ in equimolar mixture, and a salt concentration (*ca.* >1.0 M) where all the d(pA$_m$) or d(pA)$_n$ form a triple-stranded complex with d(dT)$_n$.

The complexities observed in the present case require that the contribution of the chain length to the stability of oligo–polymer interactions can be evaluated only after careful determination of the stoichiometry of the complexes formed. In the "critical region," where stoichiometry values are changing, the exact molecular stoichiometry will be indeterminate.

(11) Department of Genetics, University of Pavia, Pavia, Italy.

G. Cassani,[11] F. J. Bollum
Department of Biochemistry
University of Kentucky, Lexington, Kentucky

Di-*t*-butyl Trioxide and Di-*t*-butyl Tetroxide

Sir:

Kinetic, tracer, and product studies of autoxidation[1–4] support the sequence of reactions 1–4 as controlling chain termination. Experimental observations

$$2\text{RO}_2\cdot \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} \text{RO}_4\text{R} \quad (1)$$

$$\text{RO}_4\text{R} \overset{k_2}{\longrightarrow} [\text{RO}\cdot\text{O}_2\cdot\text{OR}] \text{ (in solvent cage)} \quad (2)$$

$$[\text{RO}\cdot\text{O}_2\cdot\text{OR}] \overset{k_3}{\longrightarrow} \text{O}_2 + \text{ROOR} \quad (3)$$

$$[\text{RO}\cdot\text{O}_2\cdot\text{OR}] \overset{k_\text{diff}}{\longrightarrow} \text{O}_2 + 2\text{RO}\cdot \quad (4)$$

(1) H. S. Blanchard, *J. Am. Chem. Soc.*, **81**, 4548 (1959).
(2) P. D. Bartlett and T. G. Traylor, *ibid.*, **85**, 2407 (1963).
(3) J. R. Thomas, *ibid.*, **87**, 3935 (1965).
(4) G. A. Russell, *ibid.*, **79**, 3871 (1957).

Figure 1. Esr signal observed at −196°.

Figure 2. Change of esr signal (calibrated against DPPH) with temperature. Below −75° changes are reversible.

Figure 3. Reversible dependence of esr signal on temperature below −75°.

on the oxidation of alkyl hydroperoxides[5] showed that (a) t-Bu$_2$O$_4$ is not stable at −70°, but (b) a compound believed to be t-Bu$_2$O$_3$ is formed at −70° and is stable up to about −35°.[6]

Di-t-butyl diperoxycarbonate,[7] irradiated with 2540-A light in frozen methylene chloride at −196° for 20 min, gave the esr signal shown in Figure 1. In contrast to the case of 2-azobis(2-phenyl-3-methylbutane),[8] no

(5) P. D. Bartlett and P. Günther, J. Am. Chem. Soc., 88, 3288 (1966).
(6) S. W. Benson, ibid., 86, 3922 (1964), has predited greater stability for RO$_3$R than for RO$_4$R.
(7) M. M. Martin, J. Am. Chem. Soc., 83, 2869 (1961).
(8) P. D. Bartlett and J. M. McBride, paper presented at the Gomberg Symposium, Ann Arbor, Mich., Aug. 23, 1966; Pure Appl. Chem., in press; see also Chem. Eng. News, 44, No. 40, 106, and No. 44, 6 (1966).
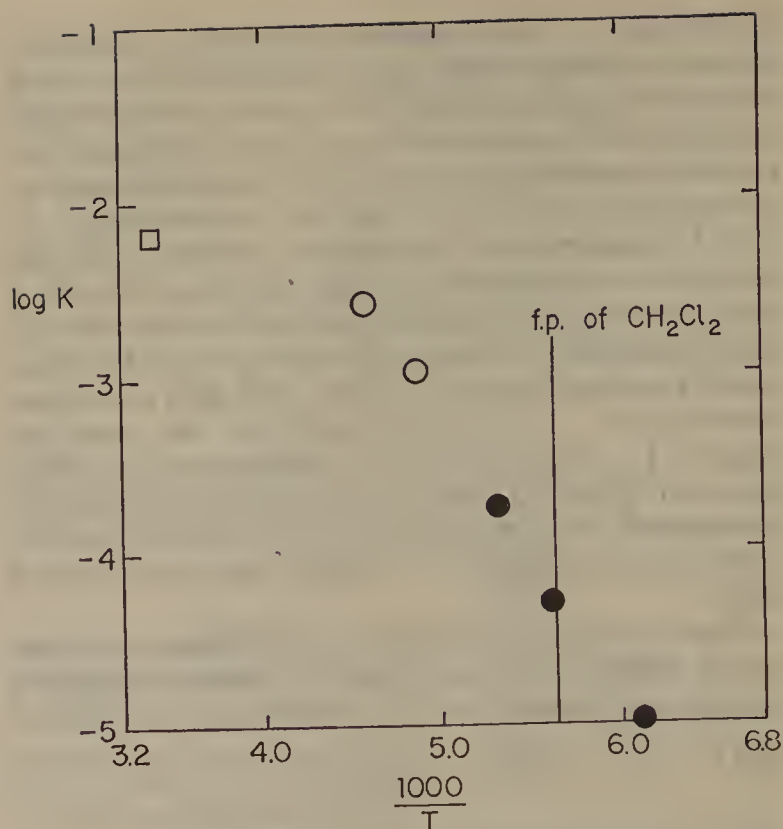
Figure 4. Dissociation constant, K, = $(RO_2 \cdot)^2/(R_2O_4)$ in CH$_2$Cl$_2$: O, from rate measurements, shortest possible extrapolation; ●, equilibrium esr, assuming complete dissociation at −75° and 6 × 10^{-5} M; □, value of Thomas,[3] from rate measurements in methanol.[10a]

triplet signal at half-field was observed. Calibrated by the radical DPPH (g = 2.0036), the signal was shown to result from overlapping of two single lines of approximate g = 2.009 and 2.016, appropriate for t-BuO· and t-BuO$_2$·. A control irradiation of pure solvent produced no esr signal.

On removal of the light and gradual warming, the esr signal passed through two minima and two maxima as shown in Figure 2. Above −120° the line was sharp, g = 2.016, the known value for the t-butylperoxy radical.[9]

The behavior of the signal from −30° up in temperature was that expected from the previous work on di-t-butyl trioxide.[5] At any constant temperature on the falling portions of the curve of Figure 2, the intensity of the signal declined with approximate second-order kinetics, according to the equations

$$\frac{-d(RO_2 \cdot)}{dt} = k_{esr}(RO_2 \cdot)^2 \qquad (5)$$

$$\log k_{esr} = \left[6.02 - \frac{1100}{T} \right] \text{l./mole sec} \qquad (6)$$

However, *in the range from −110 to −85° the signal intensity remained nearly constant at any steady temperature*, and could be increased and decreased reversibly by raising and lowering the temperature. This behavior, shown in Figure 3, indicates that the equilibrium of eq 1 adjusts itself rapidly as the temperature is altered. These observations imply that di-t-butyl tetroxide is stable only a little below the temperature (−70°) of the previous[5] oxidation of t-butyl hydroperoxide.

t-Butyl hydroperoxide, about 0.25 M, was now mixed at −90° in methylene chloride with a fourfold excess

(9) M. Bersohn and J. R. Thomas, J. Am. Chem. Soc., 86, 959 (1964).

of lead tetraacetate and allowed to stand at $-90°$ for 1.5 hr, while the lead diacetate precipitated without any oxygen evolution. The solution was then brought to constant temperatures over the range from -82 to $-68°$ and the oxygen evolution was followed kinetically. Good *first-order* lines were obtained under these conditions according to the equations

$$\frac{d(O_2)}{dt} = \frac{-d(R_2O_4)}{dt} =$$

$$k_{O_2}(R_2O_4) = k_{O_2}([O_2]_\infty - [O_2]_t) \quad (7)$$

$$\log k_{O_2} = \left[9.27 - \frac{2440}{T}\right] \sec^{-1}; \quad E_a = 11 \text{ kcal/mole}$$

$$(8)$$

The concentrated solutions prepared at $-90°$ could be frozen and cooled to temperatures as low as $-160°$ before they ceased to exhibit an esr signal. The fact that these signal levels were rapidly established and reasonably constant at each temperature below the freezing point $(-96°)$ of methylene chloride indicates considerable mobility of the tetroxide and peroxy radicals, either in a polycrystalline mixture or in pockets of concentrated solution.[10]

An estimate of the dissociation equilibrium constant $K = k_{-1}/k_1$ could be made by assuming that at 0.25 M, where k_{O_2} was measured, the tetroxide was essentially undissociated, so that k_{O_2} equals the k_2 of eq 2, and that at concentrations below 10^{-4} M, as in the measurement of k_{esr}, the dissociation is nearly complete. These assumptions, together with $k_{-1} \gg k_2$, lead to the equation

$$K = \frac{2k_{O_2}}{k_{esr}} \quad (9)$$

Combination of eq 6 and 8 then yields

$$\log K = 3.55 - \frac{1340}{T}; \quad \Delta H = 6 \text{ kcal/mole} \quad (10)$$

The two temperatures requiring the least extrapolation, -55 and $-68°$, then give values for K of 2.57 $\times$ 10^{-3} and 1.05 $\times$ 10^{-3}, respectively. The assumption that the $RO_2 \cdot$ at 6.0 $\times$ 10^{-5} M at $-75°$ was totally unassociated affords values of $K^{-85°} = 1.8 \times 10^{-4}$ and $K^{-95°} = 4.9 \times 10^{-5}$. These values are shown plotted in Figure 4, along with the estimate made in methanol by Thomas[3] by fitting his rate measurements at 22° to the equation for decomposition of the partly dissociated t-Bu_2O_4 under nonlimiting conditions. Although we might have expected the dissociation in methanol to be higher, not lower, than in methylene chloride, this value may be compatible with ours within the uncertainties of both methods.[10a]

From these values of K we calculate that in the measurement of k_{O_2} at $-68°$ and 0.25 M the dissociation was about 4.5%, while in the measurement of k_{esr} at $-55°$ and 10^{-5} M the dissociation was 99%. Thus the approximations used are adequate and yield self-consistent results.

A compound formerly thought[11] to be di-t-butyl tetroxide must be, according to its decomposition tem-

perature, the trioxide instead.[6] A stable substance reported[12] as the trioxide has been shown to be 2,2-bis-(t-butylperoxy)propane.[13,14]

(12) N. A. Milas and G. G. Arzoumanidis, *ibid.*, 66 (1966).
(13) Bartlett and Günther, ref 5, footnote 9a.
(14) R. D. Youssefyeh and R. W. Murray, *Chem. Ind.* (London), 1531 (1966).

Paul D. Bartlett, Giancarlo Guaraldi
Converse Memorial Laboratory, Harvard University
Cambridge, Massachusetts 02138
Received June 26, 1967

A Convenient Method for Stepwise Synthesis of Oligothymidylate Derivatives in Large-Scale Quantities[1,2]

Sir:

For the synthesis of high molecular weight polydeoxyribonucleotides with arbitrary, defined sequences of the four nucleotide units, methods are needed which enable one (a) to prepare and purify readily on a relatively large scale oligonucleotides or suitable oligonucleotide derivatives and (b) to utilize efficiently the oligonucleotides (or derivatives) as building blocks for construction of high molecular weight material.[3] In this communication we describe a synthetic method which satisfies stipulation a for oligothymidylate derivatives. Work is in progress to adapt the procedure to the synthesis of mixed oligonucleotide derivatives and to the construction of polynucleotides from these units.

The basic feature of the method is that chains are built with phosphotriester rather than phosphodiester links. In a final step blocking groups are removed hydrolytically to give the desired phosphodiester chains. Initial work on this approach was carried out in experiments with polymer support reactions.[4] We now find that the method can be adapted readily to work in solution, in which case the phosphotriesters can be isolated, characterized, and utilized as intermediates in subsequent synthetic steps. There are two principal advantages to the new procedure, both of which stem from the fact that the phosphotriesters obtained are uncharged, neutral molecules. (1) The products can be handled by conventional organic techniques; for example, they can be separated by chromatography with organic solvents on silica gel, which has a much higher capacity and greater flow rate than DEAE cellulose. (2) Yields do not fall off significantly as the chain length of the oligonucleotide derivative increases. As a consequence it is not necessary to employ increasingly large excesses of nucleoside reagent as the stepwise synthesis progresses.[5]

The chemistry is illustrated by the synthesis of the β-cyanoethyl-TpT derivative I, indicated in Scheme I.

(1) Part VIII in our series on nucleotide chemistry. Part VII: K. K. Ogilvie and R. L. Letsinger, *J. Org. Chem.*, 32, 2365 (1967).
(2) This research was supported by the Division of General Medical Sciences, National Institutes of Health, Grant GM-10265.
(3) For a study of the condensation of small blocks of oligonucleotides see E. Ohtsuka and H. G. Khorana, *J. Am. Chem. Soc.*, 89, 2195 (1967).
(4) R. L. Letsinger and V. Mahadevan, *ibid.*, 87, 3526 (1965); 88, 5319 (1966).
(5) See T. M. Jacob and H. G. Khorana, *ibid.*, 87, 368 (1965); S. A. Narang and H. G. Khorana, *ibid.*, 87, 2981 (1965).

(10) R. E. Pincock and T. E. Iovsky, *J. Am. Chem. Soc.*, 87, 2072, 4100 (1965).
(10a) NOTE ADDED IN PROOF. Dr. J. R. Thomas has kindly informed us that, on the basis of new evidence, his value of K shown in Figure 4 should be regarded only as a lower limit.
(11) N. A. Milas and S. M. Djokic, *Chem. Ind.* (London), 405 (1962).

Scheme I

MTr = *p*-monomethoxytrityl; Th = thymine ring

I II III TpT
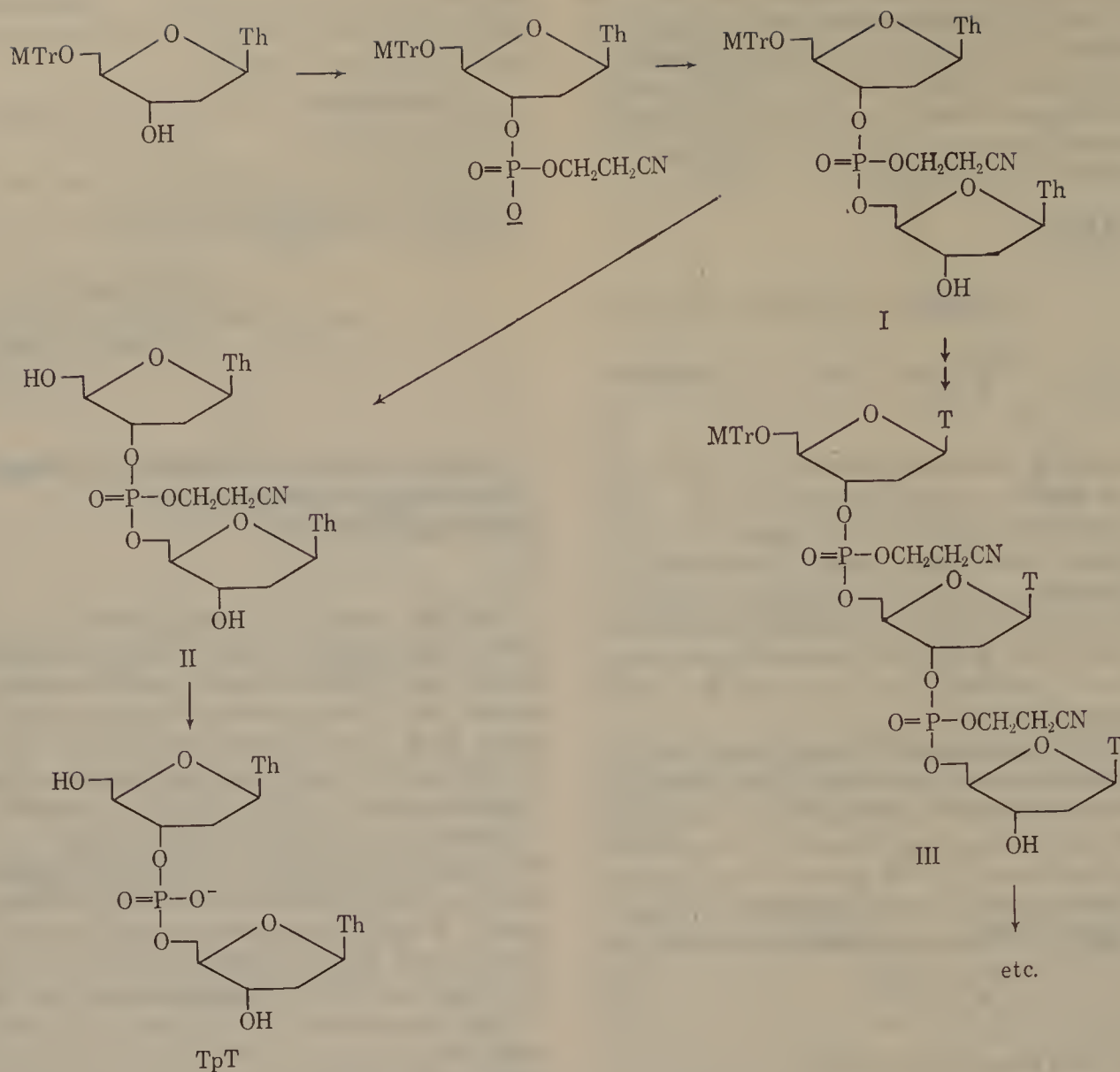
In this case 36.0 g (70 mmoles) of 5'-O-monomethoxytritylthymidine was stirred with 70 mmoles of pyridinium β-cyanoethyl phosphate and 30.5 g (140 mmoles) of mesitylenesulfonyl chloride in 140 ml of pyridine for 6 hr. Following treatment with water to hydrolyze pyrophosphates present, the phosphorylated product was extracted into chloroform, transferred to 140 ml of pyridine, and stirred with 42.5 g (140 mmoles) of triisopropylbenzenesulfonyl chloride[6] and 33.9 g (140 mmoles) of thymidine for 24 hr. The mixture was then treated with water and the solution extracted with chloroform. Two-thirds of the chloroform solution was evaporated, rediluted with chloroform, and applied to a column (100 × 3 cm) of silica gel in ethyl acetate. The column was eluted successively with 8.5 l. of ethyl acetate and 4 l. of tetrahydrofuran. Most of compound I was eluted in the first liter of tetrahydrofuran. Concentration of the tetrahydrofuran solution and addition of hexane gave I as a white solid, mp[7] 126–128°. With the material obtained from the other third of the solution, which was purified in the same manner, the yield was 39.3 g (64% based on monomethoxytritylthymidine). On warming for a few minutes with 80% aqueous acetic acid this compound was converted to

(6) R. Lohrmann and H. G. Khorana, *J. Am. Chem. Soc.*, **88**, 829 (1966).

(7) The melting points are not sharp for this series of compounds. After some preliminary softening the solid gradually becomes a glassy liquid.

the cyanoethyl derivative of thymidylylthymidine (II), mp[7] 113–115°, which in turn afforded thymidylylthymidine (TpT) cleanly on brief treatment with ammonium hydroxide at room temperature. Assay of the TpT thus obtained by hydrolysis with snake venom phosphodiesterase indicated that 96% was the desired 3'–5' isomer (hydrolysis to thymidine 5'-phosphate and thymidine) and 4% was the 3'–3' isomer (undegraded by the venom enzyme). For isolation of the pure 3'–5' isomer 7.0 g (8.0 mmoles) of I was stirred with 1.23 g (4.0 mmoles) of monomethoxytrityl chloride in 40 ml of pyridine for 20 hr. The solvent was stripped off and the products chromatographed on silica gel with ethyl acetate and tetrahydrofuran to give 6.2 g (88% recovery) of the cyanoethyl ester of 5'-O-monomethoxytritylthymidylyl-(3'–5')-thymidine, mp[7] 126–130°. The TpT obtained on removal of the methoxytrityl and cyanoethyl groups was completely hydrolyzed by an aqueous solution of the snake venom enzyme. This separation of the 3'–5' and 3'–3' isomers is based on the fact that monomethoxytrityl chloride reacts much faster with 5'-OH groups than with 3'-OH groups.

That satisfactory yields are maintained in the condensation steps as the chain is extended was demonstrated by converting I to the tetranucleoside triphosphate derivative. Thus, by essentially the same procedure used to make I, the bis(cyanoethyl) derivative of 5'-O-monomethoxytritylthymidylylthymidylylthymi-

dine (III, mp[7] 133–136°) was obtained in 49% yield from I, and the tris(cyanoethyl) derivative of 5'-O-monomethoxytritylthymidylylthymidylylthymidylylthymidine (mp[7] 144–146°) was obtained in 57% yield from III. These compounds were characterized by elemental analysis, by isolation of the de(methoxytrityl) derivatives, and by conversion to TpTpT and TpTpTpT, respectively.

Robert L. Letsinger, Kelvin K. Ogilvie
Department of Chemistry, Northwestern University
Evanston, Illinois
Received May 11, 1967

Bimolecular Substitution–Fragmentation. The Reaction of Phenylmethanesulfonyl Halides with Halide Ion

Sir:

While studying the action of nucleophilic reagents on sulfonyl halides,[1] we have encountered a new reaction of alkanesulfonyl halides exemplified by eq 1. We wish

$$PhCH_2SO_2Br \xrightarrow{Br^-} PhCH_2Br + SO_2 \qquad (1)$$

to present evidence which indicates that the reaction is simultaneously a bimolecular nucleophilic displacement on carbon and a concerted fragmentation reaction, and thereby displays mechanistic features which have not hitherto been demonstrated to exist in the same process.

Reaction 1 proceeds readily and quantitatively at room temperature in inert solvents such as methylene chloride or acetonitrile, using alkylammonium bromides as the source of bromide ion. Methanesulfonyl bromide reacts similarly but roughly $1/1000$ as fast. The analogous reaction of phenylmethanesulfonyl chloride with chloride ion also occurs, but again more slowly (see Table I).

Table I. Reaction of Sulfonyl Halides with Alkylammonium Halides in Dichloromethane at $25.0 \pm 0.1°$

Sulfonyl halide	Salt (concn, M)	k, l. mole^{-1} sec^{-1}
PhCH$_2$SO$_2$Br	Et$_4$N$^+$Br$^-$ (0.00012)	3.10×10^{-2}
PhCH$_2$SO$_2$Br	Et$_4$N$^+$Br$^-$ (0.001)	2.45×10^{-2}
PhCH$_2$SO$_2$Br	Et$_4$N$^+$Br$^-$ (0.0123)	2.35×10^{-2}
PhCH$_2$SO$_2$Br	Bu$_4$N$^+$Br$^-$ (0.00082)	2.6×10^{-2}
PhCH$_2$SO$_2$Br	Et$_3$NH$^+$Br$^-$ (0.0098)	1.53×10^{-4}
p-NO$_2$C$_6$H$_4$CH$_2$SO$_2$Br	Et$_4$N$^+$Br$^-$ (0.001)	3.85×10^{-2}
m-NO$_2$C$_6$H$_4$CH$_2$SO$_2$Br	Et$_4$N$^+$Br$^-$ (0.001)	3.50×10^{-2}
p-ClC$_6$H$_4$CH$_2$SO$_2$Br	Et$_4$N$^+$Br$^-$ (0.001)	3.15×10^{-2}
m-ClC$_6$H$_4$CH$_2$SO$_2$Br	Et$_4$N$^+$Br$^-$ (0.001)	1.72×10^{-2}
p-MeC$_6$H$_4$CH$_2$SO$_2$Br	Et$_4$N$^+$Br$^-$ (0.001)	5.26×10^{-2}
PhCH$_2$SO$_2$Cl	Et$_4$N$^+$Cl$^-$ (0.01)	1.14×10^{-4}

Reaction 1 is cleanly first order in the sulfonyl halide but only roughly so in the bromide salt, the deviation from simple second-order kinetics probably deriving to a substantial extent from ionic association.[2] *meta* or *para* substitution has a relatively small influence on the rate of reaction. The nonlinear Hammett plot

(see Table I) is akin to those that have been observed in the reaction of nucleophilic reagents with benzyl halides, thereby pointing to a SN2 mechanism.[3,4]

Consistent with this interpretation were the results from ^{13}C kinetic isotope effect studies in which it was found that the presence of ^{13}C at the benzylic carbon slowed the reaction by more than 3% at 25° ($k_{12}/k_{13} = 1.035 \pm 0.0016$).[5] A kinetic isotope effect of such a magnitude in α-phenyl-substituted systems has previously been found in bimolecular processes,[6] whereas unimolecular solvolysis of such species shows a much smaller isotope effect.[7]

Stereochemical evidence for the SN2 mechanism was obtained using (R)-phenylmethanesulfonyl-1-d bromide[8] (PhC*HDSO$_2$Br), which gave mainly the *inverted* product, (S)-benzyl-1-d bromide.[9] It is estimated that at least 60% of the product is formed by inversion, but it is not yet possible to assign a more precise value owing to uncertainty in the optical purity of the sulfonyl bromide.

There remains the question of whether the leaving anion is simply SO$_2$X$^-$ (which subsequently decomposes into SO$_2$ and X$^-$), or whether the reaction is a SN2–fragmentation process in which the S–X bond is partially broken in the transition state. The distinction between the two possible mechanisms may be summarized by structures I and II, which represent the respective transition states for the two pathways. Evidence suggesting the second mechanism is as follows. The reac-

tion of PhCH$_2$SO$_2$Cl with Et$_4$N$^+$Cl$^-$ in methylene chloride is more than 200 times slower than that of PhCH$_2$SO$_2$Br with Et$_4$N$^+$Br$^-$. Since tetraethylammonium bromide and chloride were found to be almost identical in their rate of reaction with benzyl tosylate in methylene chloride under conditions comparable to those used in the desulfonation reaction, this difference probably does not derive from a difference in nucleophilicity toward benzylic carbon between the chloride and bro-
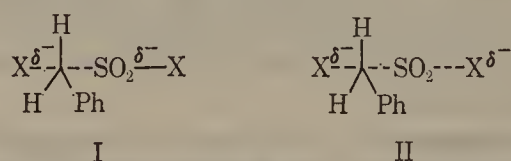
(1) Previous work: J. F. King and T. Durst, *J. Am. Chem. Soc.*, **87**, 5684 (1965); *Can. J. Chem.*, **44**, 819 (1966).

(2) *Cf.* S. Winstein, L. G. Savedoff, S. Smith, I. D. R. Stevens, and J. S. Gall, *Tetrahedron Letters*, 24 (1960), and references cited.

(3) C. G. Swain and W. P. Langsdorf, Jr., *J. Am. Chem. Soc.*, **73**, 2813 (1951); R. F. Hudson and G. Klopman, *J. Chem. Soc.*, 1062 (1962).

(4) The possibility that the benzyl halide, under favorable circumstances, might be formed *via* a sulfene was excluded by the finding that the reaction of p-nitrophenylmethanesulfonyl-1,1-d_2 bromide in the presence of triethylamine and excess Et$_3$NH$^+$Br$^-$ gave p-nitrobenzyl-1,1-d_2 bromide with no significant loss of deuterium detected.

(5) These experiments were carried out in collaboration with Dr. J. B. Stothers and Mr. A. J. McNamara, and will be described in detail at a later date.

(6) J. B. Stothers and A. N. Bourns, *Can. J. Chem.*, **40**, 2007 (1962); *cf.* also A. Fry, *Pure Appl. Chem.*, **8**, 409 (1964). Recent reinvestigation (J. B. Stothers and J. Bron, private communication) has shown that in the reaction of α-phenylethyl bromide with ethoxide ion (at 25°) $k_{12}/k_{13} = 1.030$, a higher value than that previously reported.

(7) J. B. Stothers and A. N. Bourns, *Can. J. Chem.*, **38**, 923 (1960).

(8) The sulfonyl bromide was prepared from optically active benzyl-1-d bromide by a procedure adapted from the preparation of the sulfonyl chloride described by J. L. Kice, R. H. Engebrecht, and N. E. Pawlowski, *J. Am. Chem. Soc.*, **87**, 4131 (1965).

(9) This finding, especially when taken in conjunction with our observation that the reaction is unaffected by the presence of oxygen or styrene, clearly distinguishes the halide-catalyzed reaction from the pyrolytic decomposition of alkanesulfonyl halides, which has been found to show the properties of a free-radical chain process (H. F. Herbrandson, W. S. Kelly, and J. Versnel, *ibid.*, **80**, 3301 (1958); G. Geiseler, *et al.*, *Z. Physik. Chem.* (Frankfurt), **28**, 24, 33 (1961); **33**, 264 (1962); **36**, 23 (1963)).

mide ions in this system. More striking is the observation that benzyl trifluoromethyl sulfone (PhCH₂-SO₂CF₃) does *not* react at all[10] with tetraethylammonium bromide under these conditions. A similar lack of reaction[10] was also observed with dibenzyl sulfone (PhCH₂SO₂CH₂Ph), benzyl phenacyl sulfone (PhCH₂-SO₂CH₂COPh), and phenyl phenylmethanesulfonate (PhCH₂SO₂OPh), the last being also unaffected by sodium phenoxide. To account for these observations in terms of a reaction proceeding *via* I would require that one explain why a BrSO₂⁻ group is a better leaving group than either CF₃SO₂⁻, PhCOCH₂SO₂⁻, PhOSO₂⁻, or PhCH₂SO₂⁻ by more than five orders of magnitude in each case. We find it much simpler to interpret these observations on the basis of the concerted fragmentation process (*i.e.*, *via* II), the observed rate order then reflecting the normal order of Br, Cl, CF₃, etc., as leaving anions ("nucleofugal" groups[11]).

In the light of this conclusion it is pertinent to inquire into the possibility of other concerted fragmentation processes that involve Sₙ2 reaction on carbon. A case for such a mechanism, based on $\Delta S^{\ddagger}$ values, has been made by Buncel and Millington[12] for the solvolysis of alkyl chlorosulfates. Two other reactions, the chloride ion catalyzed decomposition of alkyl chloroformates[13] and the analogous cleavage of alkyl chlorosulfites,[14] are sufficiently similar as to strongly suggest that they too may be fragmentation reactions, though direct evidence on the point is lacking at present. The twofold problem of elucidating the mechanism of the known processes and of devising and testing possible new members of this class of reactions is now under active study.

(10) Control experiments show that a reaction with $k_2 > 10^{-7}$ l. mole⁻¹ sec⁻¹ would have been readily detected. Lack of reaction in these cases therefore corresponds to a rate at least 2 × 10⁵ times slower than reaction 1.

(11) J. Mathieu, A. Allais, and J. Valls, *Angew. Chem.*, 72, 71 (1960); see also C. A. Grob and P. W. Schiess, *ibid.*, 79, 1 (1967).

(12) E. Buncel and J. P. Millington, *Can. J. Chem.*, 43, 556 (1965).

(13) J. Kenyon, A. G. Lipscomb, and H. Phillips, *J. Chem. Soc.*, 2275 (1931); D. N. Kevill, G. H. Johnson, and W. A. Neubert, *Tetrahedron Letters*, 3727 (1966).

(14) E. S. Lewis and G. M. Coppinger, *J. Am. Chem. Soc.*, 74, 308 (1952).

(15) Alfred P. Sloan Research Fellow.

J. F. King,[15] **David J. H. Smith**
Department of Chemistry, University of Western Ontario
London, Ontario, Canada
Received February 1, 1967

Bicyclo[6.2.0]deca-2,4,6,9-tetraene

Sir:

Numerous recent publications describe thermally and photolytically induced rearrangements of unsaturated hydrocarbons.[1] The behavior of the title compound (1) is of particular interest because several modes of

(1) For the bond isomerization of several C₁₀H₁₀ hydrocarbons, for instance, see (a) W. von E. Doering and J. W. Rosenthal, *J. Am. Chem. Soc.*, 88, 2078 (1966); (b) *Tetrahedron Letters*, 349 (1967); (c) M. Jones, Jr., and L. T. Scott, *J. Am. Chem. Soc.*, 89, 150 (1967); (d) E. E. van Tamelen and T. L. Burkoth, *ibid.*, 89, 151 (1967); (f) J. A. Elix, M. V. Sargent, and F. Sondheimer, *ibid.*, 89, 180 (1967).

isomerization are conceivable for this compound,[2] *e.g.* (i) ring opening to give *trans(cis)*⁴-1,3,5,7,9-cyclodecapentaene (2); (ii) subsequent rearrangement of 2 to *trans*-9,10-dihydronaphthalene (3); (iii) sigmatropic rearrangement to bicyclo[4.2.2]deca-2,4,7,9-tetraene (4);[1b,c] (iv) degenerate bond isomerization to give the same compound; (v) ring opening to afford (*cis*)⁵ cyclodecapentaene (5)[1d] followed by secondary reactions; and (vi) ring closure leading to the tricyclo compound 6 (stereochemistry unspecified). We describe herein the synthesis of this intriguing molecule and further present a preliminary account of its chemistry.[3]

A solution of bicyclo[6.1.0]nona-2,4,6-triene-*trans*-9-carboxaldehyde tosylhydrazone (7)[1c,4] in dry tetrahydrofuran containing an equivalent amount of sodium methoxide was irradiated at 0 or −30° with a Hanovia mercury lamp using a Pyrex filter. Evolution of the theoretical amount of nitrogen usually required 5–6 hr. Gas chromatography (10% silicone rubber, 90°) of the distillable product mixture provided 3, naphthalene (the combined yield of 3 and naphthalene was 45%), cyclooctatetraene (27%), 4 (7%), and a new compound (6′) (21%) (*vide infra*). This product distribution is similar to that of the thermolysis of 7 (dry salt)[1c] except that no trace of *cis*-9,10-dihydronaphthalene (8) was found in the photolysis products. When the products were kept below 0° throughout the entire work-up process[5] we obtained another new compound (1) at the expense of 3 and naphthalene.

Compound 1 (calcd mol wt for C₁₀H₁₀, 130.0783 and for C₉¹³CH₉, 130.0738; found, *m/e* 130.0758 (intensity, 20% of M − 1 base peak); calcd for C₁₀H₉, 129.0704; found, *m/e* 129.0704)[6] showed a maximum at λ_{max}^{EtOH} 258 mμ ($\epsilon \sim 1300$).[7] The nmr spectrum showed a sharp singlet at τ 3.98 (2 H) characteristic of the olefinic signal of symmetrically (σ) substituted cyclobutenes,[8] a broad singlet at τ 6.32 ascribed to two allylic protons, and other olefinic signals (6 H) at τ 4.1 to ∼4.3, similar to those of the bicyclo[6.1.0]nona-2,4,6-triene system. These spectral data are consistent with the formulation of structure 1.

(2) R. B. Woodward and R. Hoffmann, *ibid.*, 87, 395 (1965); H. C. Longuet-Higgins and E. W. Abrahamson, *ibid.*, 87, 2045 (1965); R. B. Woodward and R. Hoffmann, *ibid.*, 87, 2511 (1965).

(3) Our original aim was to prepare the carbocyclic analog of 4-azabicyclo[5.2.0]nonatriene and compare the properties of the two series of compounds; see S. Masamune and N. T. Castellucci, *Angew. Chem. Intern. Ed. Engl.*, 3, 582 (1964).

(4) The reaction product of ethyl diazoacetate and cyclooctatetraene consisted of an approximately 19:1 mixture of *trans* and all-*cis* (with respect to the substituents of the cyclopropane ring) esters. Because of the necessity of confirming the earlier stereochemical assignments [K. F. Bangert and V. Boekelheide, *J. Am. Chem. Soc.*, 86, 905, 1159 (1964)], the known acid derived from the major component was converted to cyclopropane-*trans*-1,2,3-tricarboxylic acid with permanganate-periodate. The minor acid, mp 146–147°, was isolated in pure form and the three cyclopropane ring protons showed the same chemical shift (τ 7.95): S. Masamune, unpublished.

(5) The final purification involved alumina chromatography (Woelm, neutral grade 1, pentane) followed by distillation at 0°, 0.1 mm.

(6) Taken with a direct insertion probe (MS-9) by first freezing a sample with liquid nitrogen.

(7) Compound i exhibited a maximum, λ_{max}^{hexane} 258 mμ (ϵ 1300): G. Schröder and W. Martin, *Angew. Chem. Intern. Ed. Engl.*, 5, 130 (1966).

i
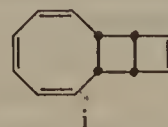
(8) For instance, see ref 3. For a revised set of coupling constants of cyclobutene itself, see E. A. Hill and J. D. Roberts, *J. Am. Chem. Soc.*, 89, 2047 (1967).

Catalytic hydrogenation of **1** with palladium on carbon or platinum provided quantitatively a saturated hydrocarbon (**9**), $C_{10}H_{18}$ (calcd mol wt, 138.1409; found, m/e 138.1409), which was found to be identical (mass, glpc, nmr, infrared) with those obtained by two alternative routes. The bis(dibromocarbene) adduct (mp 93–94°) of cycloocta-1,3-diene was treated with methyllithium at −30° [9] to afford through thermally unstable cyclodeca-1,2,4,5-tetraene a good yield of bicyclo[6.2.0]deca-1,7,9-triene (**10**). The latter compound was characterized by its nmr spectrum: τ 3.40 (sharp singlet, 2 H), 4.75–4.95 (triplet, 2 H), 7.7–7.95 (multiplet, allylic 4 H), 8.15–8.55 (multiplet, 4 H). Compound **10** was converted into **9** upon catalytic hydrogenation. Alternatively, pyrolysis of the sodium salt of bicyclo-[6.1.0]nonane-9-carboxaldehyde tosylhydrazone [10] at [160° [11] provided, in addition to cyclooctene, bicyclo-[6.2.0]dec-9-ene (calcd mol wt, 136.1252; found, m/e 136.1250); nmr, τ 4.06 (sharp singlet, 2 H), 7.1–7.4 (broad doublet, 2 H), 8.2–8.7 (multiplet, 12 H). The latter compound was subsequently converted into **9**.[12]

Compound **1** readily and *quantitatively* isomerized to *trans*-9,10-dihydronaphthalene. The rate of isomerization was measured with an approximately 0.15 M solution of **1** in deuteriochloroform and the intensity of the nmr signals at τ 6.32 of **1** and at τ 7.13 of **3** was compared at intervals, using a small sample of methylene bromide as an intensity standard. The isomerization was first order and provided the following kinetic data: $k_{42°} = (6.9 \pm 0.2) \times 10^{-5}$ sec^{-1}, $k_{70°} = (1.72 \pm 0.05) \times 10^{-3}$ sec^{-1}. In this temperature range the product **3** was essentially stable and began to change into naphthalene at a measurable rate only above 120°. An obvious proposal for this stereospecific reaction is that the C_1–C_8 bond opens in a conrotatory process to produce an unstable intermediate **2** (presumably being situated close to the transition state in the energy profile) which cyclizes in a disrotatory process at C_1 and C_6 to form **3**.[13]

Compound **6'** (calcd mol wt, 130.0783; found, m/e 130.0783) showed an nmr spectrum consisting of five complex and equally intense multiplets centered around τ 3.32, 4.08, 4.40, 6.85, and 7.53. Upon irradiation (triple) at the last two signals, the absorption at τ 3.32 and 4.40 showed an AX pattern and that at τ 4.08 collapsed to a singlet. Irradiation (triple) at the first and fourth signals produced an almost symmetrical pattern for the second and the last signals, suggesting an AA'XX' system for the latter two sets of protons. These data lead to the proposal of a tentative structure **6** for this compound. The appearance of the diallylic protons at such a high field (τ 7.53) can be rationalized by assigning the *cis,anti,cis* stereochemistry to **6'**, as indicated in **6a**. However, structure **6a** should by no means be taken as established, because other possibili-

ties such as tricyclo[5.3.0.0^{4,8}]deca-2,5,9-triene have not been rigorously excluded.

Photolysis of **1** under similar conditions to those described above[14] produced **4** in addition to other compounds. It is probable that **4** is a secondary reaction product derived from **1**. The photochemical reaction of **1** is highly complex, and we will elaborate on this subject in a separate report.
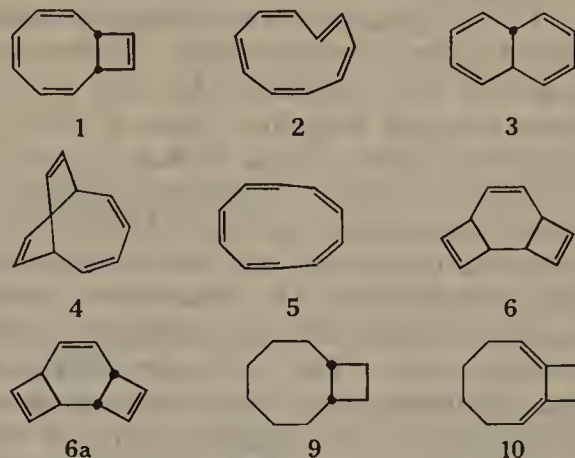
Acknowledgment. The authors are grateful to Mr. N. Nakatsuka for his skillful technical assistance, to the National Research Council of Canada for financial support, and to Badische Anilin und Soda Fabrik A.G. for a generous gift of cyclooctatetraene.

(14) Survival of **1** in the photolysis of **7** is due to the formation of insoluble sodium tosylsulfinate, which reduced greatly the transparency of the reaction medium, during the photolysis.

S. Masamune, Clinton G. Chin, Ko Hojo, Read T. Seidner
Department of Chemistry, University of Alberta
Edmonton, Alberta, Canada
Received June 26, 1967

The Reactions of Sulfur Atoms. X. Addition to Carbon–Carbon Triple Bonds and the Formation of Thiirenes

Sir:

Addition of divalent radicals such as CH_2,[1,2] O atom,[3,4] and NH[1] to acetylene results in extensive cracking and/or isomerization of the primary adduct even in low-temperature matrices. With dimethylacetylene the primary methylene addition product, dimethylcyclopropene, has been observed,[5] but the expected primary products of oxygen atom additions, the corresponding oxirenes, have never been obtained. As it appears to date, in spite of the deliberate efforts, the synthesis of the oxirene structure has not been achieved.[6] For the analogous sulfur compounds, the thiirenes, no reference can be found in the literature.[7]

We have recently examined the reactions of sulfur atoms with acetylenes utilizing a novel technique of

(9) L. Skattebøl and S. Solomon, *J. Am. Chem. Soc.*, **87**, 4506 (1965).
(10) Prepared from the corresponding carboxylic acid. This acid, prepared from cyclooctene and reported as melting at 113.5–114.8° [S. Akiyoshi and T. Matsuda, *ibid.*, **77**, 2476 (1955)], was found to contain some of the stereoisomer. The pure sample melted at 123.0–123.5°.
(11) W. Kirmse and K.-H. Pook, *Chem. Ber.*, **98**, 4022 (1965).
(12) **9** is presumably the same compound as that reported in ref 1f.
(13) Because of lack of molecular symmetry of **1**, **2**, and **3** necessary for the symmetry arguments pertaining to the above modes of isomerization, we cannot apply in a rigid sense the Woodward and Hoffmann rule[2] to these cases. However, provided that the simple MO calculation gives the correct order for the energy levels of the molecular orbitals of **5** (planar), it is predicted that **1** photolytically opens to give **5** (disrotatory) which closes thermally to *trans*-fused bicyclo[6.2.0]deca-2,4,6,9-tetraene (conrotatory) or *cis*-9,10-dihydronaphthalene (disrotatory).

(1) M. E. Jacox and D. E. Milligan, *J. Am. Chem. Soc.*, **84**, 4080 (1962).
(2) T. Terao, N. Sakai, and S. Shida, *ibid.*, **85**, 3919 (1963).
(3) C. A. Arrington, W. Brennen, G. P. Glass, J. V. Michael, and H. Niki, *J. Chem. Phys.*, **43**, 525 (1965).
(4) I. Haller and G. C. Pimentel, *J. Am. Chem. Soc.*, **84**, 2855 (1962).
(5) W. von E. Doering and T. Mole, *Tetrahedron*, **10**, 65 (1960).
(6) M. Berthelot, *Bull. Soc. Chim. France*, **14**, 113 (1879); R. N. McDonald and P. A. Schwab, *J. Am. Chem. Soc.*, **86**, 4866 (1964); W. Madelung and M. E. Oberwegner, *Ann.*, **490**, 201 (1931); W. G. Dauben, C. F. Hiskey, and M. A. Muhs, *J. Am. Chem. Soc.*, **74**, 2082 (1952); H. Schlubach and V. Franzen, *Ann.*, **577**, 60 (1952); V. Franzen, *Ber.*, **87**, 1479 (1954); J. K. Stille and D. D. Whitehurst, *J. Am. Chem. Soc.*, **86**, 4871 (1964).
(7) A. Hückel MO calculation by Zahradnik suggests a very low stability for thiirene (R. Zahradnik, *Advan. Heterocyclic Chem.*, **5**, 14 (1965).

flash photolysis with kinetic mass spectrometry, which permitted the time-resolved detection and relative concentration measurement of the inherently unstable transient thiirene and its methyl and trifluoromethyl derivatives. A preliminary account of the equipment has been given earlier.[8]

Mixtures of COS (200–400 mtorr) with acetylene (propyne, butyne-2, and hexafluorobutyne-2) (400–800 mtorr) in 14-torr He carrier were flash photolyzed, and time-resolved parent mass intensities of the expected primary adduct were recorded. In each case strong signals were obtained with the following approximate decay half-lives: $C_2H_2S \sim 2$ sec, $C_3H_4S \sim 5$ sec, $C_4H_6S \sim 7$ sec, $C_4F_6S > 0.1$ sec. These long life-time values immediately eliminate excited or radical-like carriers leaving only the thioketene[9] and thiirene structures as reasonable alternatives. The thioketene formation would require an intramolecular hydrogen, methyl, or trifluoromethyl shift. The hydrogen shift may be facile, but the methyl and especially trifluoromethyl shifts are not; yet product yields appeared to increase with increasing methyl substitution. An additional product observed with the mass spectrometer was thiophene. This compound was also found in the products of conventional photolysis experiments where the yields were 50% for C_4F_6 and 5–10% for the other acetylenes. For thiophene to be formed via the ketenes a reversal of the hydrogen or methyl shift would be required. This process should be least likely for perfluorobutyne-2, yet the thiophene yield from this compound is the highest. Thus these findings also support the thiirene vs. the thioketene structure for the primary adduct.

A much greater stability of the thiirenes relative to the oxirenes can be predicted on the basis of estimated enthalpy changes (kilocalories/mole) for the reactions

$$C_2H_2 + O \xrightarrow{-57} \underset{O}{C{=}C} \xrightarrow{-71} CH_2{=}CO \xrightarrow{68} CH_2 + CO$$

$$C_2H_2 + S \xrightarrow{-33} \underset{S}{C{=}C} \xrightarrow{-41} CH_2{=}CS \xrightarrow{105} CH_2 + CS$$
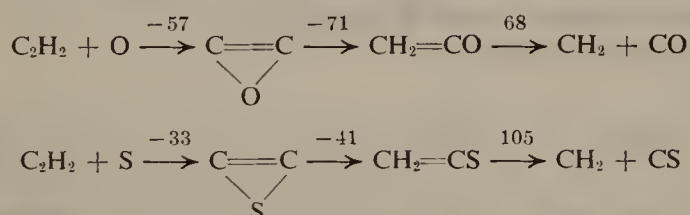
The greater tendency of the oxygen compound for isomerization and cracking is undoubtedly related to the much greater strength of the carbonyl as compared to the thiocarbonyl linkage. Cracking of the thioketene would be endothermic by 31 kcal with ground-state sulfur atoms and 5 kcal with S(^{1}D) atoms.

If present, the thioketene or its secondary photolysis product, the CS radical, should be detectable by kinetic absorption spectroscopy.[10] Therefore (1:1) mixtures of COS with acetylene and butyne-2 were flash photolyzed and the absorption spectra were recorded photographically. The spectra indicated only trace quantities of CS from the acetylene reaction and no absorbing

species at all from the butyne-2. Combining all evidence we assign the thiirene structure to the primary adduct.

The observation that the cyclic addition product of sulfur atom with acetylene is readily stabilized while the corresponding products of the oxygen and methylene addition are not is in line with the general behavior of the sulfur atom + olefin system. Thus, while the methylene + olefin[11] ($\Delta H \sim 80$ kcal) and oxygen + olefin[12] ($\Delta H \sim 84$ kcal) systems readily undergo 1,2 hydrogen (alkyl) shift to yield an olefin or a carbonyl compound, in the sulfur atom + olefin ($\Delta H \sim 60$ kcal) system it has not been possible to find evidence for a similar process.[13] Since in both the olefin and acetylene systems the isomerization implies a similar 1,2 shift, activation energies should have similar values, probably greater than 60 kcal.

Additional indirect support for the preceding arguments comes from the thermal behavior of the cyclic compounds, cyclopropane,[14] ethylene oxide,[15] and ethylene episulfide.[16] Cyclopropane and ethylene oxide readily transform by 1,2 shift to propylene and acetaldehyde while ethylene episulfide gives only ethylene and sulfur.

The over-all mechanism was further substantiated by photolysis of 1,2,3-thiadiazole (I) and 5-methyl-1,2,3-

$$\underset{I}{\overset{\displaystyle \underset{\substack{CH-N \\ CH\quad N \\ \diagdown S \diagup}}{}}{}} \xrightarrow{h\nu} C_2H_2S + N_2$$
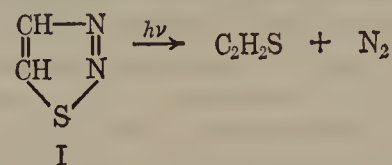
thiadiazole (II). Conventional photolysis gives only

$$\underset{II}{\overset{\displaystyle \underset{\substack{CH-N \\ CH_3\; C\quad N \\ \diagdown S \diagup}}{}}{}} \xrightarrow{h\nu} C_3H_4S + N_2$$
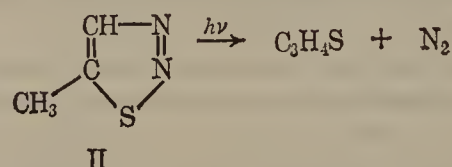
nitrogen, the corresponding acetylene, and a polymeric solid as principal products, but in the presence of perfluorobutyne-2 good yields of the 2,3-bis(trifluoromethyl)thiophenes are obtained.

Thiophene may arise by either of the steps

$$\underset{C}{\overset{C}{\|\|}} + \underset{C}{\overset{C}{\diagdown}}S \xrightarrow{(a)} \left[\underset{C-C}{\overset{C-C}{\| \quad \|}}S\right] \rightarrow \underset{C=C}{\overset{C=C}{\diagdown}}S. \xleftarrow{(b)} \underset{}{\overset{C}{C\diagdown\| }}S + \underset{C}{\overset{C}{\|\|}}$$

The reaction of sulfur atom with mixtures of C_2H_2 and perfluorobutyne-2 afforded only the asymmetrical, mixed 2,3-bis(trifluoromethyl)thiophene, favoring path b. Photolysis of I in the presence of perfluorobutyne-2 gave also only 2,3-bis(trifluoromethyl)thiophene. Photolysis of II under similar conditions yielded 2,3-bis(trifluoromethyl)-5-methylthiophene as the sole thiophene product, in agreement with path b. This also sheds further light on the nature of the intermediate since intervention of the ketene structure would be ex-

(8) W. J. R. Tyerman, W. B. O'Callaghan, P. Kebarle, O. P. Strausz, and H. E. Gunning, J. Am. Chem. Soc., 88, 4277 (1966).

(9) The synthesis of thioketene was reported by H. G. Howard (U. S. Patent 3,035,030 (1962); Chem. Abstr., 57, 13617f (1962)), but no structural identification was made. The monomer is stable at −80° but polymerizes upon warming.

(10) The thiocarbonyl group exhibits relatively strong absorption bands in the visible and near ultraviolet and the thioketene structure should also be a strong absorber. Cf. E. Campaigne in "The Chemistry of the Carbonyl Group," S. Patai, Ed., Interscience Publishers, Inc., New York, N. Y., 1966, p 936, and C. N. R. Rao, "Ultraviolet and Visible Spectroscopy," Butterworth and Co. (Publishers) Ltd., London, 1961.

(11) W. B. De More and S. W. Benson, Advan. Photochem., 2, 219 (1964).

(12) R. J. Cvetanovic, ibid., 1, 115 (1963).

(13) H. E. Gunning and O. P. Strausz, ibid., 4, 143 (1966).

(14) B. S. Rabinovitch, E. W. Schlag, and K. B. Wiberg, J. Chem. Phys., 28, 504 (1958).

(15) M. L. Neufeld and A. T. Blades, Can. J. Chem., 41, 2956 (1963).

(16) E. M. Lown, H. E. Gunning, and O. P. Strausz, to be published.

pected to lead to 2,3-bis(trifluoromethyl)-4-methyl-thiophene formation.
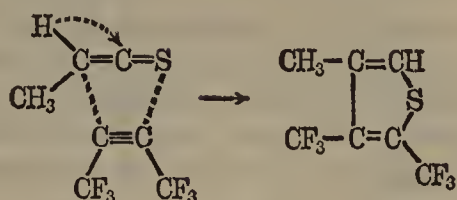
A more detailed account of these studies will be forthcoming.

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O. P. Strausz, J. Font, E. L. Dedio
P. Kebarle, H. E. Gunning
Department of Chemistry, University of Alberta
Edmonton, Alberta, Canada
Received May 18, 1967

Epimerization of 2,4-Diphenylpentane, an Oligomer of Polystyrene

Sir:

The frequency of incidence of the various conformations of a chain molecule such as a vinyl polymer HCH_2CHRCH_2CHR-, etc., or an oligomer thereof, is determined by bond torsional potentials and by interactions between nonbonded atoms. These interactions occur in profusion if R is a group as large as or larger than CH_3. The same factors must determine the equilibrium distribution among the various diastereoisomers generated by racemization of the asymmetric centers CHR. A statistical mechanical theory of stereochemical equilibrium in chain molecules containing asymmetric centers has been developed recently on this basis.[1] The same parameters that serve to describe the relative proportions of various conformers for a given stereoisomer also define the equilibrium distribution over the various diastereomeric species. Methods for racemization of the asymmetric centers in molecules of the type considered, and for accurate analysis of the equilibrated mixture, are therefore of immediate relevance to investigation of the incidence of various conformations which a given species may assume.

In pursuit of this objective we have succeeded in establishing conditions for equilibration of the *meso* and *dl* isomers of 2,4-diphenylpentane in dimethyl sulfoxide (DMSO) containing potassium *t*-butoxide. The ready occurrence of proton transfer reactions between hydrocarbons under these conditions has been demonstrated in a number of instances.[2,3] By analogy to these investigations, racemization of the asymmetric centers of 2,4-diphenylpentane may be presumed to occur *via* the formation of a planar alkyl-substituted benzyl anion.[2]

meso- and *dl*-2,4-diphenylpentanes were synthesized by the method of Overberger and Bonsignore.[4] The diastereoisomers were partially separated[5] and quanti-

tatively determined[6] by gas chromatography. Nmr spectra[7] of the compounds agreed with published results.[8,9] The equilibrium ratios shown in the final column of Table I represent averages of triplicate

Table I. Epimerization of *meso*- and *dl*-2,4-Diphenylpentane

Sample	Initial % *meso*	Equilibration Time, days	% *meso*
1	70.0	7	56.5[a]
2	45.0	14	48.4
3	29.5	14	48.4
4	84.5	28	48.5

[a] Not fully equilibrated.

analyses[10] which were in mutual agreement within ±0.5%; other values reported are the means of duplicate measurements.

The compounds were epimerized by layering the reagents in a narrow tube in the following order: potassium *t*-butoxide, DMSO, and a mixture of the hydrocarbon with DMSO. The contents were immediately frozen, then degassed, and the tube was sealed. Mixing of the different layers upon gradual warming to room temperature produced a pink color which persisted until the tube was opened and the base destroyed by the addition of water. The color, which disappears rapidly on exposure to air, is indicative of a benzyl anion.[11] The hydrocarbon was extracted with pentane, a poor solvent for DMSO, and analyzed. From the final values of the % *meso* given in the last column of Table I, it is evident that the epimerization has reached equilibrium after 14 days and that the same final composition, 48.4% *meso*, is attained from both directions.

In order to confirm that the response of the flame ionization detector used for the gas chromatographic analysis was directly proportional to the concentration of the two isomers, an equilibrated mixture was independently analyzed by taking its nmr spectrum in CCl_4 using the Varian HR-100 spectrometer, the instrument being tuned with special care. The proportions of the two isomers were calculated from the areas of the respective methyl peaks[12] as determined by the triangle approximation. They were also computed from the peak heights. The latter method has been shown to be valid for a series of diastereomeric esters.[13] Both methods gave 47 ± 1% *meso* for the composition of the equilib-

(1) P. J. Flory, *J. Am. Chem. Soc.*, 89, 1798 (1967).
(2) D. J. Cram, "Fundamentals of Carbanion Chemistry," Academic Press Inc., New York, N. Y., 1965.
(3) J. E. Hoffman, R. J. Muller, and A. Schriesheim, *J. Am. Chem. Soc.*, 85, 3002 (1963).
(4) C. G. Overberger and P. V. Bonsignore, *ibid.*, 80, 5427 (1958).
(5) Aerograph Model A90-P3 chromatograph, Varian Aerograph Inc., Walnut Creek, Calif. A column, 20 ft × ³/₈ in., packed with 20% by weight FFAP on Chromosorb W operated at 240° with helium as the carrier gas was used.
(6) Aerograph Model 600-D chromatograph with flame ionization detector. A column, 12 ft × ¹/₈ in., filled with 20% Apiezon-L on acid-washed Firebrick was used. Optimum separation was achieved at 230° with a helium flow rate of 75 cc/min.
(7) Varian A-60 spectrometer operated at room temperature with approximately 20% (w/v) solutions in CCl_4 and tetramethylsilane as reference.
(8) F. A. Bovey, F. P. Hood III, E. W. Anderson, and L. C. Snyder, *J. Chem. Phys.*, 42, 3900 (1965).
(9) D. Lím, B. Obereigner, and D. Doskočilová, *J. Polymer Sci.*, B3, 893 (1965).
(10) Calculations of the two isomers based on the areas of the respective peaks measured with a planimeter.
(11) G. A. Russell and A. G. Bemis, *J. Am. Chem. Soc.*, 88, 5491 (1966).
(12) The methyl doublets of *meso*- and *dl*-2,4-diphenylpentane are centered respectively at δ 1.20 and 1.15.
(13) J. A. Dale and H. S. Mosher, to be published.

rium mixture, a result which agrees with the analysis by gas chromatography within the combined experimental errors. Gas chromatographic analysis is believed to be the more reliable method.

The only conformers of the *meso* isomer not precluded by severe steric overlaps are the *trans,gauche* (*tg*), i.e.

tg
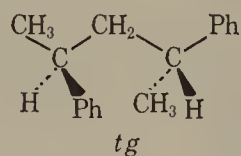
and its analog (*gt*) of opposite screw sense. The eligible conformations of the racemic isomer are *tt* and *gg*, i.e.,

tt   *gg*
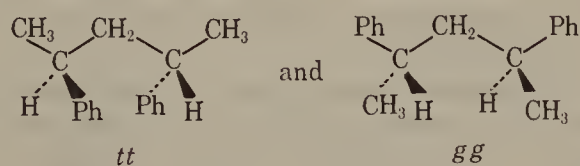
Let η denote the statistical weight for a conformation in which phenyl is *gauche* with respect to a CH group separated from it by three skeletal bonds. This statistical weight is to be assigned relative to a statistical weight of unity for a CH_3 group similarly situated with respect to CH. On this basis the combined statistical weight for the two equivalent *meso* conformers is 2η; the statistical weights for the *tt* and *gg* conformers of the racemic form are η^2 and 1, respectively. Hence, the fraction of *meso* at equilibrium[1] is $f_{meso} = 2\eta/(1 + \eta)^2$. Taking $f_{meso} = 0.48$ as a weighted mean of the experiments here reported, $\eta = 1.5$ at 25°.[14] The *tt* conformer of the racemic isomer is predicted to be favored over the *gg* by the factor $\eta^2 = 2.25$. At the same temperature the ratio of these two conformers deduced from nmr spectra interpreted in terms of coupling constants is *ca.* 3.0 according to Bovey[8] and Doskočilová[15] and their co-workers, in satisfactory agreement with our deductions.

At least one additional parameter is required for the interpretation of the stereochemical equilibrium and the distribution among conformers for any higher homolog.[1] Analysis of the epimerization equilibrium for the next homolog, namely, 2,4,6-triphenylheptane, should yield this parameter and also test the validity of the scheme presented elsewhere.[1] Experiments directed to this end are in progress, along with investigation of the epimerization of polystyrene. These results and their implications concerning the conformations of vinyl chain molecules will be subjects of future publications.

(14) The other root, $\eta = 0.667$, of the quadratic equation for f_{meso} has been dismissed on the grounds that it is irreconcilable with the preference for the *tt* conformer of the racemic isomer.

(15) D. Doskočilová, S. Sýkora, H. Pivcová, B. Obereigner, and D. Lim, *J. Polymer Sci.*, in press.

Alan D. Williams, John I. Brauman
Norvell J. Nelson, Paul J. Flory
Department of Chemistry, Stanford University
Stanford, California 94305
Received May 11, 1967

The Structure of Streptozotocin

Sir:

Streptozotocin,[1-4] an antibiotic produced by *Streptomyces achromogenes*, is a broad spectrum antibacterial agent and also has antitumor activity in both *in vitro* and *in vivo* systems. We wish to present evidence supporting the assignment of structure I to streptozotocin.

I, R = H
II, R = $COCH_3$
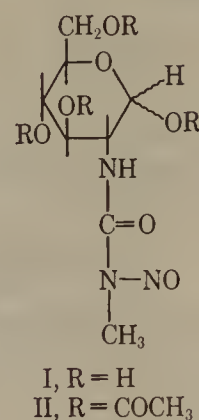
Streptozotocin has the molecular formula[5,6] $C_8H_{15}N_3O_7$ and decomposes with evolution of gas at *ca.* 115°. The molecular weight determined by isothermal distillation in water is 269 (calcd, 265). Potentiometric titration showed the absence of any titratable groups. The nmr spectrum[7] of streptozotocin could not be completely interpreted; however, it showed the presence of an $N-CH_3$ group (singlet, 3 H, at δ 3.15) and the absence of any $C-CH_3$ groups.

Acetylation of streptozotocin with acetic anhydride and pyridine afforded crystalline tetraacetate II, $C_8H_{11}N_3O_7(COCH_3)_4$, $[\alpha]^{25}D +41°$ (*c* 0.78, 95% ethanol), mp 111–114° dec. The nmr spectrum of II showed the presence of four O-acetyl groups (12 H, δ 1.97–2.08) and the $N-CH_3$ group which is also present in streptozotocin.

Treatment of the antibiotic with alkali (2 *N* aqueous NaOH) at 0° resulted in the evolution of diazomethane,[8] and carbon chromatography of the neutralized reaction mixture resulted in the isolation of III as an amorphous colorless solid, $C_7H_{11}NO_6$, $[\alpha]^{25}D -40°$ (*c* 1, water). III exhibited infrared absorption at 1725 cm^{-1} and yielded carbon dioxide and D-glucosamine hydrochloride, $C_6H_{13}NO_5 \cdot HCl$, by treatment with 2 *N* aqueous HCl. Treatment of the alkali degradation reaction mixture with acetic anhydride and pyridine afforded IV, a crystalline colorless solid, $C_7H_7NO_6(COCH_3)_4$, mp 178–180° (uncor), $[\alpha]^{25}D -46°$ (*c* 0.7, 95% ethanol). Acid hydrolysis of IV (2 *N* HCl, reflux) again yielded D-glucosamine hydrochloride and carbon dioxide. The infrared spectrum (carbonyl absorption at 1790 and 1745 cm^{-1}) and the nmr spectrum (3 H, singlet, at δ

(1) J. J. Vavra, C. DeBoer, A. Dietz, L. J. Hanka, and W. T. Sokolski, *Antibiot. Ann.*, **1959–1960**, 230 (1960).

(2) W. T. Sokolski, J. J. Vavra, and L. J. Hanka, *ibid.*, **1959–1960**, 241 (1960).

(3) C. Lewis and A. R. Barbiers, *ibid.*, **1959–1960**, 247 (1960).

(4) R. R. Herr, T. E. Eble, M. E. Bergy, and H. K. Jahnke, *ibid.*, **1959–1960**, 236 (1960).

(5) Analytical values for all the compounds described in this paper are consistent with the indicated formulas.

(6) The molecular formula was previously reported as $C_{11}H_{27}N_5O_{12}$,[4] based on early molecular weight determinations.

(7) Nmr spectra were observed in dimethylformamide-d_7 on a Varian A-60 spectrometer using internal tetramethylsilane as a reference.

(8) Diazomethane was collected in ether and this solution was mixed with an ether solution of *p*-nitrobenzoic acid. Crystalline methyl *p*-nitrobenzoate isolated was identical with an authentic sample.

CH_2OH ... CH_2OAc

III ... IV, Ac = COCH_3
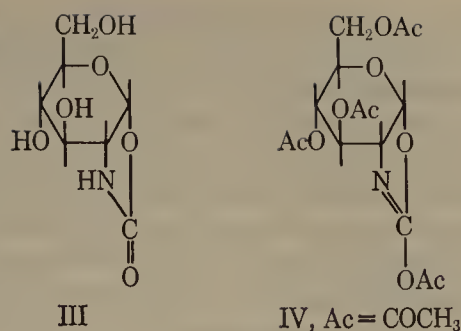
2.48; three singlets, 3 H each, at δ 1.97, 2.03, and 2.07) of the tetraacetate IV are consistent with the postulation of the presence of an enol acetate grouping in IV.

The formation of diazomethane and a positive Liebermann nitroso test[9] suggested the presence of an N-nitrosomethylamide group in streptozotocin. The absence of a free amino group in streptozotocin, together with the isolation of carbon dioxide and D-glucosamine from acid hydrolysis of III or IV, indicate the nitrosoamide to be present as a urea derivative involving the nitrogen of the glucosamine. This conclusion is consistent with both the ultraviolet [λ_{max} 228 mμ (ϵ 6360)][10] and the infrared spectra (carbonyl absorption at 1700 cm^{-1},[11,12] $-NN=O$ at 1530 cm^{-1} [13]) of streptozotocin. These data establish the structure of streptozotocin as I.

Various lots of crystalline streptozotocin as isolated, identical in all other respects, have shown wide variations in optical rotation ([α]^{25}D +15 to 68°). However, aqueous solutions of these samples rapidly undergo mutarotation to an equilibrium value of [α]^{25}D 39°. This indicates that streptozotocin is a mixture of α and β anomers with the C$_1$-hydroxyl unsubstituted.

The structure of streptozotocin was confirmed by its synthesis. Tetra-O-acetylglucosamine hydrochloride[14] (V) treated with methyl isocyanate[15] gave VI, C$_{16}$H$_{24}$N$_2$O$_{10}$, mp 142–144°, [α]^{25}D +18° (c 0.9, 95% ethanol). Attempts to deacetylate VI prior to nitrosation, using

CH_2OAc ... V ... CH_2OAc ... VI

MeOH, NH_3 / room temperature

NOCl / pyr

CH_2OH ... VII

II $\xrightarrow[-10°]{\text{MeOH} \atop \text{NH}_3}$ streptozotocin (I)

(9) W. J. Hickinbottom, "Reactions of Organic Compounds," 2nd ed, Longmans, Green and Co., Ltd., London, 1948, p 358.
(10) A. I. Scott, "Interpretation of the Ultraviolet Spectra of Natural Products," The MacMillan Co., New York, N. Y., 1964, p 41.
(11) L. J. Bellamy, "The Infra-red Spectra of Complex Molecules," John Wiley and Sons, Inc., New York, N. Y., 2nd ed, 1958, p 223.
(12) The reported value for amide carbonyl absorption in substituted ureas is 1660 cm^{-1}.[11] However, the presence of the electronegative N-nitroso group is expected to reduce the contribution of the ionic form of the amide and as a result the carbonyl frequency is raised. A similar effect may account for the high frequencies of N-nitrosoamides which absorb near 1740 cm^{-1} in solution.[13]
(13) E. H. White, J. Am. Chem. Soc., 77, 6008 (1955).
(14) M. Bergmann and L. Zervas, Ber., 64B, 975 (1931).
(15) F. Micheel and W. Lengsfeld, ibid., 89, 1246 (1956).

ammonia in methanol (room temperature), afforded only the cyclic product VII, C$_8$H$_{14}$N$_2$O$_5$,[16] mp 177–178°, [α]^{25}D $-21°$ (c 0.77, water). VII, which shows no reducing properties, has also been obtained from streptozotocin by treatment with 0.1 N aqueous sulfamic acid; 1 mole of N$_2$/mole of I is evolved during this reaction. Treatment of VI with nitrosyl chloride in pyridine[17] afforded tetraacetylstreptozotocin (II) identical with an authentic sample. Ammonolysis of II in methanol ($-10°$) afforded streptozotocin identical in all respects with that obtained from fermentations.

In addition to streptozotocin, S. achromogenes produces enteromycin[18,19] and U-15,774,[19] both compounds containing unusual nitrogen functions.

(16) This cyclization of the methyl ureido compound is contrary to the results reported by C. J. Morel, Helv. Chim. Acta, 44, 403 (1961), who did not obtain the cyclic product during ammonolysis of several other alkyl derivatives, but is analogous to the results reported by both Morel and Micheel[15] with aryl derivatives.
(17) M. S. Newman and A. Kutner, J. Am. Chem. Soc., 73, 4199 (1951).
(18) K. Mizuno, Bull. Chem. Soc. Japan, 34, 1419, 1425, 1631, 1633 (1961).
(19) P. F. Wiley, R. R. Herr, F. MacKellar, and A. D. Argoudelis, J. Org. Chem., 30, 2330 (1965).

R. R. Herr, H. K. Jahnke, A. D. Argoudelis
Research Laboratories, The Upjohn Co.
Kalamazoo, Michigan
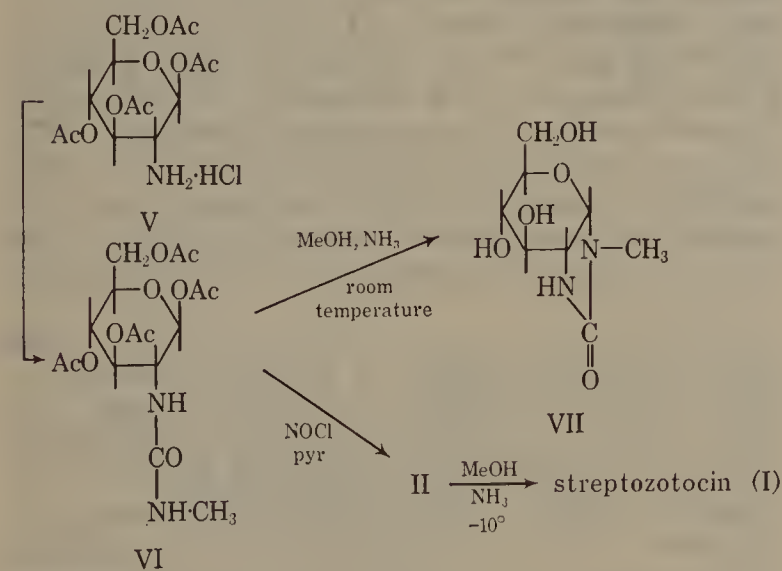Received June 9, 1967

Metal Ion Facilitation of Atom-Transfer Oxidation–Reduction Reactions[1]

Sir:

Reactions of transition metal compounds can often be classified in analogous patterns, from which new reactions can be deduced. The efficacy of this approach is illustrated by the oxidative addition reactions of d^8 [2,3] and d^{10} [4] systems. Herein we propose another class of transition metal reactions: metal ion promoted atom-transfer oxidation–reduction reactions.

Consider a molecule or ion X–Y reacting with a molecule or ion Z to form products X–Z and Y such that atom (or group) transfer takes place, X–Y being reduced and Z being oxidized (eq 1).

$$X-Y + Z \longrightarrow X-Z + Y \tag{1}$$

A partial list of potential oxidizing agents X–Y includes RN$_3$, N$_3^-$, RCHN$_2$, RNCNR, RNO$_2$, NO$_2$, NO$_2^-$, NO, NO$^+$, ArN$_2^+$, N$_2$O, SeO$_2$, O$_3$, O$_2$, H$_2$O$_2$, ROOR, and ROOH.[5] Reducing agents Z might include H$^-$, R$^-$, RC≡C:$^-$, RC≡CR, RCH=CHR, R$_3$P, CO, RNC, CN$^-$, N$_3^-$, SO$_2$, and SnCl$_2$.[6] Most of the possible permutations afford thermodynamically allowed reactions; however, many combinations lack a low-energy

(1) This research was supported by the National Science Foundation and the Advanced Research Projects Agency, Contract SD 100.
(2) (a) L. Vaska and S. S. Bath, J. Am. Chem. Soc., 88, 1333 (1966); (b) P. B. Chock and J. Halpern, ibid., 88, 3511 (1966).
(3) J. P. Collman and W. R. Roper, ibid., 87, 4008 (1965); 88, 3504 (1966).
(4) C. D. Cook and G. S. Jauhal, Can. J. Chem., 45, 301 (1967).
(5) In a few instances atom transfer takes place from the reducing agent to the oxidizing agent rather than the converse which is shown in eq 1.
(6) Ligands are written in their uncoordinated state.

pathway to allow the reaction to occur under moderate conditions. It is our hypothesis that incorporation of both reactants (X–Y and Z) into *cis* positions of the coordination sphere of a metal complex might provide a mechanism to facilitate such atom-transfer redox reactions. In cases where reactants X–Y and Z replace products X–Z and Y in the coordination sphere, the over-all process would be homogeneously catalyzed by a metal complex. Such reactions may also be heterogeneously catalyzed by chemisorption.

Our first encounter with such a process was the reaction of acyl or aryl azides with iridium(I) or rhodium(I) carbonyl complexes (1) to form organic isocyanate or

$$MCl(CO)L_2$$
1a, M = Rh
b, M = Ir
L = triphenylphosphine

nitrogen complexes (only the iridium nitrogen complex is stable enough to be isolated).[7] Addition of CO regenerates the original carbonyl complex (1) which can then react with more organic azide so that the over-all process is catalytic (eq 2). The activation energies are

$$ArN_3 + CO \xrightarrow[\text{MCl(CO)L}_2 \text{ (1)}]{} ArNCO + N_2 \qquad (2)$$

small and these reactions are rapid at low temperatures. Coordinatively saturated iridium carbonyl complexes do not react with organic azides under these mild conditions, illustrating the requirement of incorporating both oxidizing and reducing agent in the metal coordination sphere. In the absence of a metal complex, CO and organic azides do not react at a measurable rate.

A related process is the stoichiometric reaction of the iridium(I) and rhodium(I) carbonyl azides (2) with CO to yield the corresponding isocyanates (3)[8] (eq 3). The bisazido complexes of palladium and platinum (4) undergo a similar transformation (eq 4).[9] The parallel

$$MN_3(CO)L_2 + CO \longrightarrow MNCO(CO)L_2 + N_2 \qquad (3)$$
2a, M = Rh   **3**
b, M = Ir

$$M(N_3)_2L_2 + CO \longrightarrow M(NCO)_2L_2 + 2N_2 \qquad (4)$$
4a, M = Pd   **5**
b, M = Pt

$$NaN_3 + Pd\text{–}C + CO \xrightarrow{H_2O} NaOCN + N_2 \qquad (5)$$

between homogeneous and heterogeneous catalysis is demonstrated by the reaction of sodium azide, carbon monoxide, and palladium on charcoal to form the sodium cyanate (eq 5).

Incorporation of azide and CO into *cis* positions or within close proximity in the coordination sphere is insufficient to cause the reaction to occur (at least at ambient temperatures). Thus the hydrogen, oxygen, and diethyl acetylenedicarboxylate adducts[8] derived from the iridium carbonyl azide 2 are stable and do not undergo spontaneous atom-transfer redox reactions.

Among examples of metal ion promoted atom-transfer redox reactions from the recent literature, carbon monoxide is the reducing reagent in several instances. Aryl nitro compounds oxidize CO to CO$_2$ and form iso-

cyanates in the presence of rhodium(I) complexes[10] and palladium or rhodium metal.[11] Nitrobenzene reacts with iron pentacarbonyl to form carbon dioxide and azo and nitroso compounds.[12] In the latter case thermal or photochemical activation is required to produce a coordinatively unsaturated metal complex. The reaction of water with carbon monoxide in the presence of PdBr$_3^-$ has been recently reported.[13] Nitrite ion also reacts with coordinated CO to form CO$_2$ (as complexed carbonate) and coordinated NO.[14]

Among potential oxidizing agents perhaps the most intriguing is molecular oxygen. It has been proposed that coordinated oxygen is peroxidic on the basis of increased oxygen–oxygen bond length[15] and on the formation of hydrogen peroxide upon protonation.[16,17] Catalytic oxidation of tertiary phosphines[17,18] and isonitriles[18] by O$_2$ using complexes derived from d^{10} systems have been described. Similarly, oxidation of SO$_2$ to coordinated SO$_4^{2-}$ and NO$_2$ to coordinated NO$_3^-$ has been recently reported.[19,20] We have found that NO reacts with the platinum(II)–oxygen complex 6[17,21] to form the bisnitro complex 7 (eq 6).

$$PtO_2L_2 + NO \longrightarrow Pt(NO_2)_2L_2 \qquad (6)$$
6   **7**

Olefins are significant reducing agents in the above list. We report here the catalysis of autoxidation of cyclohexene and cyclopentene by complexes of d^8 metals (eq 7). Using oxygen pressures of 14–36 psi at 25–60° and catalyst concentrations of 10^{-2} M in benzene

$$\qquad (7)$$

IrI(CO)L$_2$ IrCl(N$_2$)L$_2$ RhClL$_3$
8   **9**   **10**

or methylene chloride, oxidation of 20 to 50% of 2–5 g of cycloolefin was observed in 24 hr. Cyclohexen-3-one[22a,b] and water[22a] were identified as major products of the autoxidation of cyclohexene: cyclohexene oxide[22a,b] and other as yet unidentified compounds were minor products. Cyclopentene oxide[22a] was also identified as a minor product in the oxidation of cyclopentene. It is likely that 3-cyclohexene hydroperoxide is an intermediate in the above reaction, but this has not

(10) British Patent 993,704 (June 2, 1965); Dutch Patent 6,502,601 (Nov 25, 1965). We are indebted to R. P. Bennett, American Cyanamid Co., for calling our attention to these references.

(11) W. B. Hardy and R. P. Bennett, *Tetrahedron Letters*, 961 (1967).

(12) (a) E. A. Koerner von Gustorf, Abstracts, 153rd National Meeting of the American Chemical Society, Miami, Fla., April 1967, p L43; (b) J. E. Kimlick, *J. Org. Chem.*, 30, 2014 (1965).

(13) G. G. Kutyokov, A. B. Fasman, A. E. Lyutŝ, Yu. A. Kushnikov, V. F. Vozdvizhenskii, and V. A. Golodov, *Russ. J. Phys. Chem.*, 40, 798 (1966).

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(15) J. A. McGinnety, R. J. Doedens, and J. A. Ibers, *Science*, 145, 709 (1967).

(16) L. Vaska, *ibid.*, 140, 809 (1963).

(17) G. Wilke, H. Schott, and P. Heimbach, *Angew. Chem. Intern. Ed. Engl.*, 6, 92 (1967).

(18) S. Takahashi, K. Sonogashira, and N. Hagihara, *J. Chem. Soc. Japan*, 87, 610 (1966).

(19) J. J. Levison and S. D. Robinson, *Chem. Commun.*, 198 (1967).

(20) C. D. Cook and G. S. Jauhal, *J. Am. Chem. Soc.*, 89, 3066 (1967).

(21) C. D. Cook and G. S. Jauhal, *Inorg. Nucl. Chem. Letters*, 3, 31 (1967).

(22) (a) Identified by comparison of their glpc retention time with that of authentic samples; (b) identified by comparison of their mass spectra with those of authentic samples.

(7) J. P. Collman, M. Kubota, J.-Y. Sun, and F. Vastine, *J. Am. Chem. Soc.*, 89, 169 (1967).

(8) Satisfactory elemental analyses and infrared spectra have been obtained for these compounds.

(9) After completion of our study of reactions 4, similar results were reported by W. Beck and W. P. Fehlhammer, *Angew. Chem. Intern. Ed. Engl.*, 6, 169 (1967).

been verified.[23] With the exception of the rhodium complex **1a**, the other active catalysts[15,24] are known to form complexes with molecular oxygen. It is significant that the iridium chloride complex **1b** is a poor catalyst for the autoxidation in benzene solution, but the analogous iodide complex **8** is an effective catalyst. Apparently, olefins such as cyclohexene displace oxygen from the coordination sphere in **1b**, and the resulting olefin complex is less likely to coordinate with oxygen. It is probable that a prerequisite for this oxidation is prior coordination of molecular oxygen. The iodide **8** is known to form a much more stable oxygen adduct than the chloride **1b**.[2b,15]

(23) Such an intermediate has been suggested in the autoxidation of olefins catalyzed by iron phthalocyanine: A. H. Cook, *J. Chem. Soc.*, 1774 (1938).

(24) J. A. Osborn, F. H. Jardine, J. F. Young, and G. Wilkinson, *J. Chem. Soc., Sect. A*, 1711 (1966).

(25) Author to whom inquiries should be addressed: Department of Chemistry, Stanford University, Stanford, Calif. 94305.

(26) National Science Foundation Science Faculty Postdoctoral Fellow, 1966–1967.

James P. Collman,[25] Mitsuru Kubota,[26] John W. Hosking
Venable Laboratory, University of North Carolina
Chapel Hill, North Carolina
Received June 19, 1967

Novel Diazoalkanes and the First Carbene Containing the (MeO)₂P(O) Group

Sir:

The preparation of diazoalkanes containing heteroatom substituents, *e.g.*, $(RS)_2CN_2$,[1] $(PhSO_2)_2CN_2$,[2] $ROCH_2CHN_2$,[3] and RSO_2CHN_2,[4] their preparative utilization, and their decomposition to carbenes have been of current interest. Diazoalkanes containing phosphorus substituents, $Ph_2P(O)C(Ph)N_2$[5] and $R_2P(O)CHN_2$ (R = Ph, $PhCH_2$),[6] have been reported also.

We have prepared $(MeO)_2P(O)C(Ph)N_2$ (I) and $(MeO)_2P(O)C(Me)N_2$ (II) because we felt that they would serve excellently, *via* the great variety of reactions diazoalkanes and the carbenes (or carbenoids) derived from them are capable of undergoing, in the introduction of organophosphorus functionality into diverse organic and inorganic compounds. We felt that I and II would be more useful than the $Ph_2P(O)$-substituted diazoalkanes since their methoxy groups represent reactive phosphorus functionality which would be useful in further synthetic steps.

Compounds I and II were synthesized as shown in eq 1. Compound I is an orange-red, crystalline solid, mp 44–44.5°, which could be distilled at reduced pressure and which appears to be stable indefinitely at room temperature. Compound II is a yellow, distillable liquid, bp 37–38° (0.13 mm), $n^{25}D$ 1.4583, which decomposes slowly at room temperature but is quite stable on storage at 0°. Both compounds show infrared bands characteristic of the diazo group, I at 2080 and II at 2075 cm⁻¹, as well as P–O absorption at 1260 cm⁻¹.

(1) U. Schöllkopf and U. Wiskott, *Ann. Chem.*, **694**, 44 (1966).

(2) J. Diekmann, *J. Org. Chem.*, **28**, 2933 (1963).

(3) C. Grot, E. Pfeil, E. Weinrich, and O. Weissel, *Ann. Chem.*, **679**, 42 (1964).

(4) A. M. Van Leusen, R. J. Mulder, and J. Strating, *Rec. Trav. Chim.*, **86**, 225 (1967), and earlier publications of this research group.

(5) L. Horner, H. Hoffmann, H. Ertel, and G. Klahre, *Tetrahedron Letters*, 9 (1961).

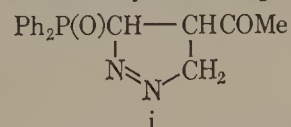(6) N. Kreutzkamp, E. Schmidt-Samoa, and A. K. Herberg, *Angew. Chem.*, **77**, 1138 (1965).

$$\left(\begin{array}{l} R = Ph, 94\% \\ R = Me, 55\% \end{array}\right)$$ (1)
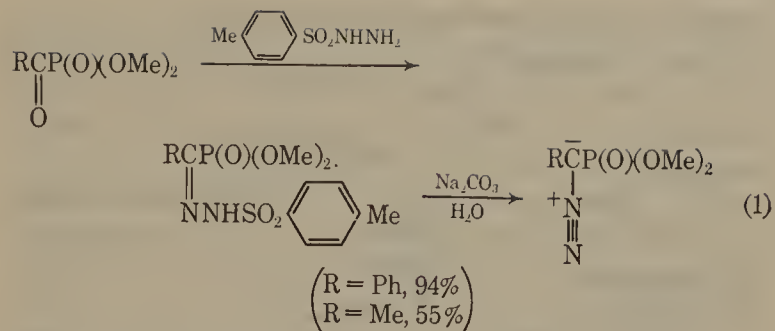
The unusually high stability of $Ph_2P(O)$- and $(MeO)_2P(O)$-substituted diazoalkanes is noteworthy and may be a consequence of $C \rightarrow P \pi$ bonding. Compounds I and II have proved to be versatile reagents, undergoing the usual diazoalkane reactions and also showing carbenoid reactivity on treatment with copper powder. Scheme I summarizes reactions of I, Scheme II reac-

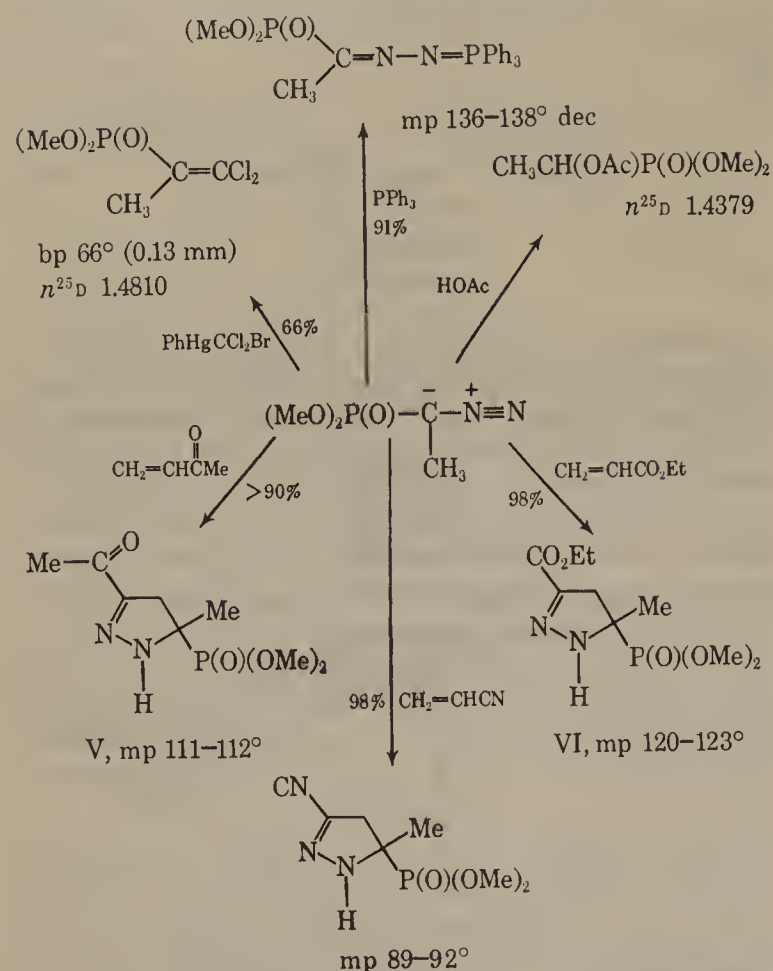**Scheme I.** Reactions of $(MeO)_2P(O)C^-(Ph)N_2^+$
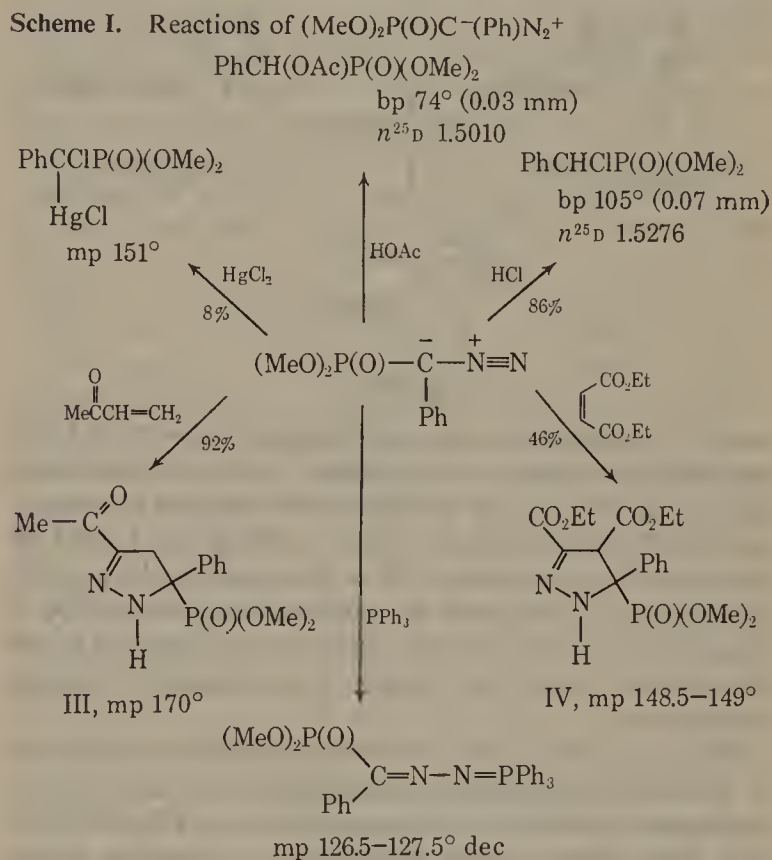
tions of II. The products of 1,3-dipolar addition of I and II to activated vinyl compounds appear to be 2-pyrazolines as shown; where two modes of addition are possible, the isomer involving Michael addition of the diazo carbon is favored. All 1,3-dipolar adducts showed strong N–H infrared absorption at ~3200 cm⁻¹ and a broad downfield singlet in the nmr spectrum, which was assignable to the N–H proton. Adducts to methyl vinyl ketone and ethyl acrylate showed carbonyl absorption corresponding to α,β unsaturation: $\nu_{C=O}$ (cm⁻¹): III, 1660; V, 1655; VI, 1725. The diethyl maleate adduct IV showed two distinct C=O peaks at 1725 and 1735 cm⁻¹, demonstrating the presence of conjugated and unconjugated carbonyl groups.[7] Of special interest in Scheme II is the reaction of II with phenyl(bromodichloromethyl)mercury in refluxing ben-

(7) Kreutzkamp, *et al.*,[6] reported that additions of $Ph_2P(O)CHN_2$ to methyl vinyl ketone and dimethyl maleate give 1-pyrazolines, *e.g.*, i,
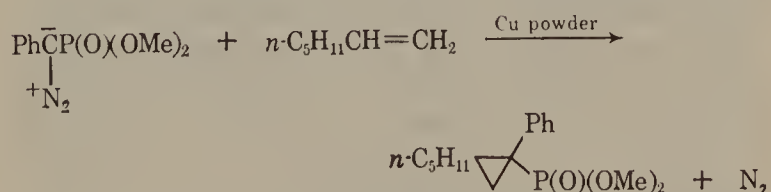

but unfortunately provided no spectroscopic evidence in support of their structural assignments, so that their correctness cannot be assessed.

Scheme II. Reactions of $(MeO)_2P(O)C^-(CH_3)N_2^+$

ples of the generation and trapping of a phosphorus-substituted carbene.

All compounds mentioned in this communication gave combustion analyses and infrared and/or nmr spectra in agreement with the structures indicated. Our efforts in this general area are continuing.

(9) Alfred P. Sloan Foundation Fellow, 1962–1966.
(10) Postdoctoral Research Associate, 1965–1966.
(11) National Institutes of Health Predoctoral Fellow, 1966–1967.

Dietmar Seyferth,[9] **Peter Hilbert,**[10] **Robert S. Marmor**[11]
*Department of Chemistry, Massachusetts Institute of Technology
Cambridge, Massachusetts 02139*
Received June 9, 1967

Structures of the Excited States of Furan Produced on Mercury ($^3P_1$) Photosensitization

Sir:

In an earlier communication[1] it had been reported that the principal reaction that was observed on sensitization of furan vapor with $Hg(^3P_1)$ atoms was decarbonylation to give a mixture of propyne and cyclopropene.[2] In an attempt to elucidate the mechanism of this reaction, the influence of a number of factors on the photosensitized reactions of furan has been studied. Evidence is presented here for the intermediacy of I and II in this system, and on this basis the structures III, IV, and V are proposed for the excited states of furan. Only one electronically excited state is possible in this system—the triplet—if the spin conservation rule is applicable. This state should possess considerable vibrational energy as well. III, IV, and V are resonance
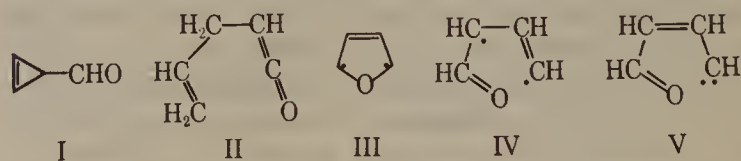
structures but their unique behavior generates considerable doubt that they are equivalent in any way in this system. IV may be an electronically excited state and III a vibrationally excited ground state formed by internal conversion. The origin of V is obscure.

Reaction of $Hg(^3P_1)$ atoms with furan at pressures which ranged from 0.2 to 1.0 atm[3] gave two compounds of formula C_7H_8O and a compound of formula $C_8H_8O_2$.[4] The first two which were presumably adducts of furan and C_3H_4 were isolated by vpc. In the infrared spectra of this pair the only absorptions that could be attributed to an oxygen function were a series of intense bands

zene. Dihalocarbene–diazoalkane reactions have been reported previously by Reimlinger,[8] and this represents the first application of this mercurial reagent in such a reaction. Notable also is the stability of I and II toward carboxylic acids. On a 10-mmole scale, a ~15-hr period of reflux of I in ethereal acetic acid (100% excess) was required for the evolution of nitrogen to be completed. I was inert to benzoic acid under the same conditions.

While a solution of I in benzene could be boiled for 48 hr without perceptible decomposition, the addition of copper powder to a benzene solution of I, followed by a 19-hr reflux period, resulted in evolution of nitrogen and a color change from orange to yellow. When a mixture of 6 mmoles of I, 60 mg-atoms of copper powder, and 100 ml of 1-heptene was heated at reflux for 12 hr, this same color change was observed. Filtration through Celite, evaporation of unconverted olefin, and distillation at reduced pressure gave 1.29 g (73%) of dimethyl 1-phenyl-2-*n*-amylcyclopropylphosphonate, bp 108° (0.04 mm), $n^{25}D$ 1.5025. A similar reaction

$$Ph\overset{-}{C}P(O)(OMe)_2 + n\text{-}C_5H_{11}CH=CH_2 \xrightarrow{\text{Cu powder}}$$
$$\underset{+N_2}{|}$$

with cyclohexene gave **VII** (stereochemistry unknown), mp 117–118°, in 65% yield. Another recrystallization from cyclohexane raised the melting point to 120–120.5°. No addition of $PhCP(O)(OMe)_2$ to tetramethylethylene or *cis*-1,2-dichloroethylene was observed. In these cases the $PhCP(O)(OMe)_2$-derived product was $(MeO)_2P(O)C(Ph)=C(Ph)P(O)(OMe)_2$, mp 187.5–188.0°. These reactions thus provide the first exam-

(8) H. Reimlinger, *Chem. Ber.*, **97**, 339, 3503 (1964).

(1) R. Srinivasan, *J. Am. Chem. Soc.*, **89**, 1758 (1967).
(2) The small amount of allene that was observed is believed to come by a secondary process, possibly photochemical.
(3) None of the products reported here are to be observed on direct irradiation of furan in solutions.
(4) The molecular weights and formulas of all of the compounds reported here were determined by analytical mass spectrometry using an AEI MS-9 instrument.

from 1000 to 700 cm⁻¹ much as in the spectrum of furan itself. The nmr spectra of these two compounds were very similar and consisted of a narrow multiplet at τ 3.63 (2 H) due to a pair of olefinic protons and another narrow multiplet at τ 5.4 ± 0.1 (2 H) which could be attributed to a pair of allylic protons situated α to an oxygen atom. The remaining four protons gave rise to a complex pattern from τ 8.4 to 9.4 in one case and 9.0 to 10.0 in the other. The chemical shifts of these protons especially in the latter instance indicated that they were located in a cyclopropyl ring. From the similarity of these spectra to those of the Diels–Alder adducts of furan that have been reported[5] it was deduced that these products have the structures VI and VII.
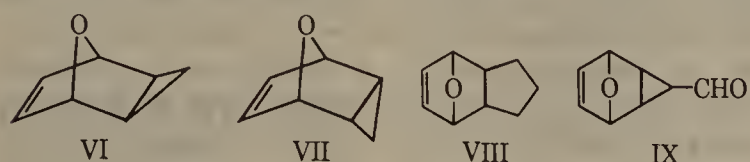
It has already been reported[5a] that the Diels–Alder addition of furan lacks the stereospecificity of cyclopentadiene so that the formation of both VI and VII is not surprising. The identification of one from the other was hindered by poorly resolved nmr spectra.

Since furan undergoes Diels–Alder addition to even an activated double bond only slowly, the possibility that this reaction is also photosensitized was considered. Photosensitization of furan in the presence of cyclopentene gave not only VI and VII but in addition a new product of the formula $C_9H_{12}O$ (infrared spectrum similar to that of VI and VII from 1000 to 700 cm⁻¹; nmr spectrum: τ 3.75 (2 H), narrow multiplet; 5.55 (2 H), multiplet; 7.9–8.7 (8 H), complex; ultraviolet λ_{max} 3000 A (ϵ_{max} 71);[6] reduction with hydrogen and Adams catalyst—uptake 1.2H_2) which was identified as the Diels–Alder adduct VIII of unknown stereochemistry. The fact that the addition of cyclopentene (18.9 mm) to furan (76.6 mm) diminished by 20% but did not scavenge the formation of CO and C_3H_4 indicated that the excited state of furan which underwent Diels–Alder addition (which is most likely to be III) was not the precursor for the decarbonylation reaction. The observed decrease can be reasonably explained by the quenching of some of the Hg($^3P_1$) atoms by cyclopentene instead of by furan.

The product of formula $C_8H_8O_2$ was isolated by column chromatography over silica gel. It showed an intense absorption in its infrared spectrum at 1710 cm⁻¹ and a weak absorption at 2750 cm⁻¹ which indicated that it was an aldehyde. The presence of a doublet at τ 0.93 (1 H; J = 7 cps) in the nmr spectrum confirmed that there was a –CHO group with a >CH adjacent to it. The rest of the spectrum consisted of a narrow multiplet at τ 3.80 (2 H), a broad multiplet at 4.95 (2 H), and two complex absorptions at 7.41 (2 H) and 8.05 (1 H), respectively. The characteristic patterns at τ 3.80 and 4.95 indicated that the product was a Diels–Alder adduct of furan to a C_4H_4O fragment which had the structure C_2H_2>CH–CHO. The shift of the car-

bonyl frequency by about 20 cm⁻¹ to longer wavelength showed a conjugation of the >C=O vibration to the rest of the molecule. The only protons that were not accounted for occurred in a pair at τ 7.41. This suggested structure IX which demonstrates that 2-cyclopropenecarboxaldehyde (I) is an intermediate in this system.[7] It is proposed that I is formed from an excited state of structure IV[8,10] and that I gives rise to cyclopropene and carbon monoxide by an intramolecular rearrangement, since oxygen decreases the yield of cyclopropene but does not eliminate it.

The possibility had been suggested[1] that furan on photosensitization may also rearrange to vinylketene II. When furan (137 mm) is allowed to react with Hg($^3P_1$) atoms in the presence of methanol (37 mm) the quantum yields for CO and cyclopropene were reduced by 13%, which decrease can be wholly attributed to the deactivation of some of the mercury atoms by methanol. At the same time the formation of a new product was observed. From spectral data this was identified as the methyl ester of vinylacetic acid, CH_2=$CHCH_2COOCH_3$ (X). Obviously, furan on photosensitization has undergone addition to methanol. The product from the addition of CH_3OD to furan under the same conditions was examined by nmr spectroscopy. In X, the absorptions at τ 4.17 (1 H), 4.76 (2 H), 6.33 (3 H), and 7.00 (2 H) can be attributed to the –CH–, terminal methylene, methyl, and allylic protons. In the monodeuterated ester the absorptions at these τ values corresponded to 0.98, 2.01, 3.00, and 1.10 protons, respectively. The adduct must therefore be CH_2=$CHCHDCOOCH_3$ (XI). If the ester is formed from vinylketene II by the addition of CH_3OD this distribution of deuterium would be readily explicable. An alternative mechanism in which the excited-state structure III reacts with methanol would predict an incorrect distribution of deuterium. It would appear that furan is capable of transiently forming vinylketene II and the probable excited state (V) which is the precursor for this reaction is not the same as III or IV.

It is important to point out here that decarbonylation is the significant photosensitized process in furan and that the products formed by the other pathways have a quantum yield of one-fifth to one-tenth of this value. However, the identification of these alternate pathways helps to understand the mechanism of the decarbonylation reaction.

Acknowledgment. The author wishes to thank Mr. Fred Hetzel for the nmr spectra and Dr. Harold Shechter for much useful advice and many helpful discussions.

(7) The dimethyl derivative corresponding to the aldehyde I (actually a methyl ketone) has recently been isolated from the 2,5-dimethylfuran–Hg($^3P_1$) system. It has a half-life of about 3 days at −10°.

(8) It is noteworthy that such a ring contraction has been reported before in the photochemistry of 3,5-diphenylisoxazole.[9] In this case, the initial isomerization leads to a phenyl ketone which was actually isolated.

(9) E. F. Ullman and B. Singh, (J. Am. Chem. Soc., 88, 1844 (1966).

(10) Although such ring contractions have not been observed in thiophene, H. Wynberg and his co-workers (ibid., 88, 5047 (1966)) have indicated that a similar mechanism may be used to explain certain photoisomerizations in that system.

(11) Address inquiries to the IBM Watson Research Center, Yorktown Heights, N. Y. 10598

R. Srinivasan[11]
Evans Chemical Laboratory, Ohio State University
Columbus, Ohio 43210
Received May 31, 1967

(5) (a) F. A. L. Anet, *Tetrahedron Letters*, 1219 (1962); (b) M. P. Kunstmann, D. S. Tarbell, and R. L. Autrey, *J. Am. Chem. Soc.*, 84, 4115 (1962); (c) P. E. Eaton and K. Lin, *ibid.*, 87, 2052 (1965).

(6) There is no obvious explanation for this ultraviolet absorption. Both VI and VII also display ultraviolet absorption maxima at 3020 (ϵ_{max} 340) and 3050 A (ϵ_{max} 350) which are consistent with the formulation of their structures as being related to VIII.

Temperature Dependence of Photoisomerization. IV. Evidence for the Involvement of Triplet States in the Direct Photoisomerization of Stilbenes

Sir:

Contrary to the opinion expressed recently,[1,2] we wish to suggest that the direct photoisomerization of stilbenes proceeds following intersystem crossing from the first excited singlet level S_1 into an isoenergetic or quasi-isoenergetic triplet level T. We base this conclusion on several different lines of experimental evidence.

1. External Enhancement of the trans-to-cis Photoisomerization Quantum Yield in Stilbene at Low Temperatures by a Heavy-Atom Solvent. The above quantum yield ϕ_t in *fluid* hydrocarbon solutions, with light at 313 mμ, decreases from 0.50 at room temperature to 0.006 at $-183°$.[3,4] This decrease is equivalent to an activation energy of about 1.2 kcal/mole, assumed to be equal to the energy gap between the vibrationally relaxed first excited singlet level (S_1) and a quasi-isoenergetic triplet level (T) into which crossing takes place.[5a] In an outgassed fluid methylcyclohexane–isohexane (MCH/IH) solution of stilbene (3×10^{-5} M) at $-105°$, ϕ_t is[4] 0.12. The fluorescence quantum yield, ϕ_F, of *trans*-stilbene under the same conditions is[5b] 0.54 ± 0.08. In fluid solutions in *n*-butyl bromide, serving as a heavy atom solvent (dried over Al_2O_3 *in vacuo*), under the same conditions, ϕ_t is 0.49 ± 0.05 and ϕ_F is 0.30 ± 0.05. Thus in a heavy-atom solvent at $-105°$ ϕ_t retains its value at room temperature, while ϕ_F is smaller than in MCH/IH. We explain these results by assuming an enhanced yield of intersystem crossing ϕ_{ISC} by the heavy atom, an effect well known from other cases[6,7] and ascribed to mixing between the singlet and triplet states of the solute. In the present case an increased mixing would result either in a depression of the level T or in an increased probability of intersystem crossing to a different triplet level T', of energy lower than T.

2. Internal Enhancement of ϕ_t Values at Low Temperatures by Substituents (either a heavy atom or groups with a low energy localized $n-\pi^*$ triplet transition).[5a] We have found that in sterically nonhindered stilbenes, in fluid media, the temperature dependence of ϕ_t is determined by the nature of the substituent on the aromatic ring. Stilbene proper and its derivatives substituted with a group showing only a weak effect on intersystem-crossing yields, such as 4-chloro-, 4-methoxy-, or 4-dimethylaminostilbene, require an activation energy (from 1 to 10 kcal/mole) for the intersystem-crossing steps. In these compounds the ϕ_t values (0.3–0.6 at room temperature) decrease to almost zero at low temperatures. Stilbenes substituted with groups that enhance intersystem crossing[8] have ϕ_t values independent on temperature. This behavior was observed in 4-bromostilbene[3,4] and 4-nitro-, 4-aceto-, and 4-benzoylstilbene.[5a] We propose that the reason for this effect

and for the external enhancement is similar, namely, an enhanced yield ϕ_{ISC}.

3. Uncoupling of the Fluorescence from the trans-to-cis Photoisomerization by Using High-Viscosity Media. The ϕ_t values of stilbene and many of its sterically unhindered derivatives are strongly lowered in media of very high viscosity,[5b] while the ϕ_F values are practically unaffected. Thus for stilbene in glycerol at $-80°$ $\phi_t = 0.001$ and $\phi_F = 0.46$, while in MCH/IH[5a,9] $\phi_t = 0.22$ and $\phi_F = 0.35$. For 4-bromostilbene in glycerol at $-80°$ the respective values are $\phi_t = 0.009$ and $\phi_F = 0.11$, while in MCH/IH at the same temperature[4] $\phi_t = 0.35$ and ϕ_F 0.11. We have ascribed[5b] this effect to the fact that *cis*-stilbene occupies a larger volume than *trans*-stilbene in solution, and that the increase in volume during *trans → cis* transformation cannot be accommodated in a highly viscous solvent. Under such conditions isomerization stops while its precursor, intersystem crossing, continues and remains the major pathway competing with fluorescence in the deactivation of the first excited singlet of *trans*-stilbene.

A genuine quenching of the S_1 level of stilbenes would not detract in any way from the validity of the present conclusions about the triplet mechanism. However, the interpretation of the quenching experiment of excited stilbene molecules by azulene[1] is somewhat controversial. Azulene was reported *as a very efficient quencher of triplets*,[10] while tris(dibenzoylmethanato)-iron(III), which is known as an efficient quencher of singlet excited molecules, does not affect the unsensitized photoisomerization.[11,12]

The lack of any effect of perdeuteration on the rate of direct photoisomerization, and on the photostationary composition of the system stilbene + sensitizer, at room temperature, was suggested[2] as evidence against the triplet mechanism of direct photoisomerization. We have confirmed these results with stilbene perdeuterated in the rings and obtained similar ones in a wide temperature range, down to $-180°$, both for ϕ_t and ϕ_F. However, we believe that this absence of an isotope effect is definitely compatible with a triplet mechanism. In stilbenes, the $T_1 \rightarrow S_0$ decay (during or following which the final geometry is determined) takes place by a mechanism different from that of the radiationless transition $T_1 \rightarrow S_0$ in rigid polycylic aromatic molecules, as described by Robinson and Frosch.[13] Thus in stilbenes a crossover, without tunneling, from a common T_1 state (configuration proper to zero-point energy) to a twisted S_0 state is energetically feasible.[3,11] Moreover, results of photosensitization experiments[11] and the absence of phosphorescence in stilbenes[14,15] indicate that this $T_1 \rightarrow S_0$ radiationless transition has a very high rate constant which, contrary to the stituation with rigid aromatic molecules,

(1) J. Saltiel, E. D. Megarity, and K. G. Kneipp, *J. Am. Chem. Soc.*, 88, 2336 (1966).
(2) J. Saltiel, *ibid.*, 89, 1037 (1967).
(3) R. H. Dyke and D. S. McClure, *J. Chem. Phys.*, 36, 2326 (1962).
(4) S. Malkin and E. Fischer, *J. Phys. Chem.*, 68, 1153 (1964).
(5) Forthcoming publications in this series: (a) part V; (b) part VI.
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(7) S. P. McGlynn, M. J. Reynolds, G. W. Daigre, and N. D. Christodoyleas, *J. Phys. Chem.*, 66, 2499 (1962).
(8) S. K. Lower and M. A. El-Sayed, *Chem. Rev.*, 66, 199 (1966).

(9) Interpolation of the results of ref 4, Figure 1.
(10) G. S. Hammond and P. A. Leermakers, *J. Phys. Chem.*, 66, 1148 (1962).
(11) G. S. Hammond, J. Saltiel, A. A. Lamola, N. J. Turro, J. S. Bradshaw, D. O. Cowan, R. C. Counsell, V. Vogt, and C. Dalton, *J. Am. Chem. Soc.*, 86, 3197 (1964).
(12) *Cf.* R. P. Foss and D. O. Cowan, unpublished results, mentioned on p 3211 of ref 11.
(13) G. W. Robinson and R. P. Frosch, *J. Chem. Phys.*, 38, 1187 (1963).
(14) F. Aurich, M. Hauser, E. Lippert, and H. Stegemeyer, *Z. Physik. Chem.* (Frankfurt), 42, 123 (1964).
(15) A. A. Lamola, G. S. Hammond, and F. B. Mallory, *Photochem. Photobiol.*, 4, 259 (1965).

does not depend on the overlap factor between the vibrational wave functions of the T_1 state and the isoenergetic, C–H vibrationally excited S_0 level. It is the latter which is strongly affected by deuteration. The magnitude of the energy gap $T_1 \rightarrow S_0$, which otherwise determines the overlap factor,[13] may therefore be expected to be without any effect on the high rate of the radiationless $T_1 \rightarrow S_0$ process.

We conclude that positive evidence in favor of triplet intermediates is available, whereas evidence against them is either disputable or not relevant.

K. A. Muszkat, Dina Gegiou, Ernst Fischer
Chemistry Department, Weizmann Institute of Science
Rehovoth, Israel
Received June 2, 1967

Conformational Flexibility of Thianthrene and Its Oxides[1]

Sir:

Thianthrene, the *cis-* and *trans-*5,10-dioxides, and the 5,5,10,10-tetroxide have folded structures in the crystal state,[2] with dihedral angles in the neighborhood of 130°. While dipole moment evidence[3,4] indicates that folding about the line joining the sulfur atoms is maintained in solution, it is recognized that the molecule of thianthrene and its derivatives oscillates rapidly through a planar position, as deduced from theoretical estimates[5–7] (3–7 kcal/mole) of the activation energy barrier which separates the folded molecule of thianthrene from its inverted form, from failure to separate the stereoisomers which result from folding,[5,8] and from dipole moment[4] and nmr[9] studies. Similar conclusions have been arrived at from studies of analogous heterocyclic systems.[6,8,10,11]

In light of the overwhelming evidence attesting to conformational flexibility in thianthrene and its derivatives, a recent report by Janczewski and Charmas[12] assumes particular importance. The finding by these authors

(1) This work was supported by the Air Force Office of Scientific Research under Grant No. AF-AFOSR-1188-67.
(2) H. Lynton and E. G. Cox, *J. Chem. Soc.*, 4886 (1956); I. Rowe and B. Post, *Acta Cryst.*, 11, 372 (1958); S. Hosoya and R. G. Wood, *Chem. Ind.* (London), 1042 (1957); S. Hosoya, *ibid.*, 159, 980 (1958); S. Hosoya, *Acta Cryst.*, 16, 310 (1963); 21, 21 (1966).
(3) E. Bergmann and M. Tschudnowsky, *Ber.*, 65, 457 (1932); W. S. Walls and C. P. Smyth, *J. Chem. Phys.*, 1, 337 (1933); G. M. Bennett and S. Glasstone, *J. Chem. Soc.*, 128 (1934); T. W. J. Taylor, *ibid.*, 625 (1935); E. Bergmann and A. Weizmann, *Chem. Ind.* (London), 364 (1938); H. Lumbroso and G. Montaudo, *Bull. Soc. Chim. France*, 2119 (1964).
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(11) The conformational rigidity ascribed to conformers of 9-[(N-methyl-3-piperidyl)methyl]thioxanthene (W. Michaelis, O. Schindler, and R. Signer, *Helv. Chim. Acta*, 49, 42 (1966)) is more properly described by the statement that one of the two forms (i.e., the a',a' form in the *cis* isomer and the a',e' form in the *trans* isomer) exists as by far the most populous component in a *mobile* conformational equilibrium.[6]
(12) M. Janczewski and W. Charmas, *Roczniki Chem.*, 40, 1243 (1966); for a preliminary report, see ref 13.
(13) M. Janczewski, M. Dec., and W. Charmas, *ibid.*, 40, 1021 (1966).

that oxidation of the optically active forms[13] of *cis-* and *trans-*2-thianthrenecarboxylic acid 5,10-dioxide (1) affords optically active 2-thianthrenecarboxylic acid 5,5,10,10-tetroxide (2) is of far-reaching significance, for the following reasons. Isolation of optically active disulfone 2 demonstrates unequivocally that the tricyclic structure is *rigidly* folded; the resistance of 2 to racemization under the drastic conditions of preparation (oxidation of 1 with 30% hydrogen peroxide in glacial acetic acid at 105–115° for 5 hr) and purification (recrystallization from boiling glacial acetic acid) shows that a surprisingly high energy barrier (*i.e.*, of the order of 25 kcal/mole or greater[14]) separates the enantiomeric conformers of 2; and the observation[12] that (+)-*cis*-1 and (+)-*trans*-1 both give (+)-2 with $[\alpha]^{20}\text{D}$ +18.18° while (−)-*cis*-1 and (−)-*trans*-1 both give (−)-2 with $[\alpha]^{20}\text{D}$ −18.18° can only mean that both *cis-* and *trans-*sulfoxides 1 contain the two possible diastereomeric conformers in *identical* ratios. The last point is illustrated in Chart I, with arbitrarily chosen configurations and con-

Chart I

| cis-1 | trans-1 | 2 |
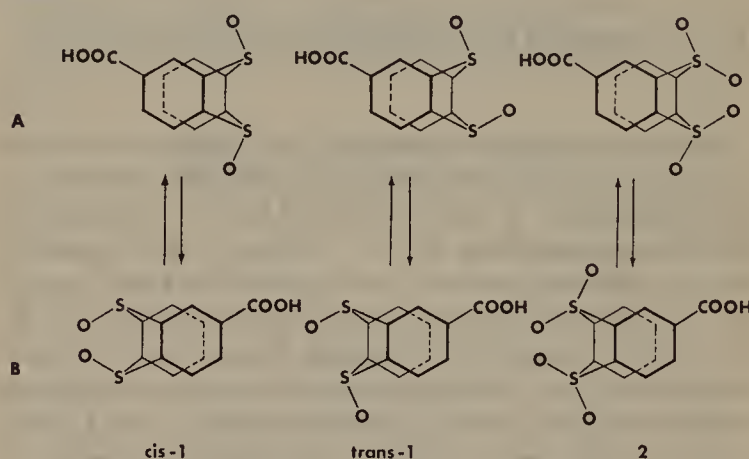
formations: only the same ratio of *cis*-1A:*cis*-1B and of *trans*-1A:*trans*-1B can result in the same ratio of (+)-2:(−)-2, *i.e.*, in the same optical rotation of 2. Alternatively, the conformers of *cis-* and *trans-*1 must exist predominantly in one of the two possible forms (*e.g.*, A), exhibiting a thermodynamic preference which is particularly unexpected for *trans-*1.

We now report that the claims[12] of Janczewski and Charmas cannot be substantiated. The preparation and resolution of *cis-* and *trans-*1 were repeated, giving results in essential agreement with those reported.[13] When racemic *cis*-1 was heated for 5 hr with 30% hydrogen peroxide in glacial acetic acid at 105–115°, the product (±)-2 had mp 306–308° (lit.[12] 312–314°, lit.[13] 300–301°, lit.[15] 302–303°) and an infrared spectrum identical with that reported.[12] *Anal.* Calcd for $C_{13}H_8O_6S_2$: C, 48.14; H, 2.49; S, 19.77. Found: C, 48.32; H, 2.44; S, 19.86; M⁺, m/e 324. Oxidation of (−)-*cis*-1 (mp 278–280° with resolidification and remelting at 296–298°[16], $[\alpha]^{25}\text{D}$ −134° (1% aqueous sodium hydroxide); lit.[13] mp 285–287°, $[\alpha]^{20}\text{D}$ −126.57° (1% aqueous sodium hydroxide)) under the same condi-

(14) For example, taking the half-life of racemization as 10 min at 105°, if $\Delta S\ddagger = 0$ eu, $\Delta H\ddagger = 27.3$ kcal/mole.
(15) H. Gilman and D. R. Swayampati, *J. Am. Chem. Soc.*, 79, 208 (1957).
(16) At the melting point the optically active forms of *cis-* and *trans-*1 suffer racemization by pyramidal inversion at sulfur (cf. D. R. Rayner, E. G. Miller, P. Bickart, A. J. Gordon, and K. Mislow, *ibid.*, 88, 3138 (1966)); furthermore, the *trans* form isomerizes to the *cis* form (K. Mislow, P. Schneider, and A. L. Ternay, Jr., *ibid.*, 86, 2957 (1964)), mp 296–298°.

tions[12] afforded a product identical in melting point and infrared spectrum with (±)-2, α^{20}D 0.00 ± 0.01° (c 0.684, $l=2$, 1% aqueous sodium hydroxide),[17] α^{27}_λ 0.000 ± 0.001° in the region 600–310 nm (c 0.317, $l=0.1$, 1% aqueous sodium hydroxide).[18] Identical results were obtained starting from (+)-trans-1 (mp 252–253° with resolidification and remelting at 296–298°,[16] [α]^{25}D +41.2° (1% aqueous sodium hydroxide); lit.[13] mp 262–264°, [α]^{20}D +40.17° (1% aqueous sodium hydroxide)).

The expected conformational flexibility of the thianthrene tetroxide system has thus been demonstrated, and the contrary conclusions[12] are invalidated.

(17) Schmidt and Haensch visual polarimeter.
(18) Cary Model 60 automatic recording spectropolarimeter.
(19) Public Health Service Postdoctoral Fellow, 1967.

James Chickos,[19] Kurt Mislow
Department of Chemistry, Princeton University
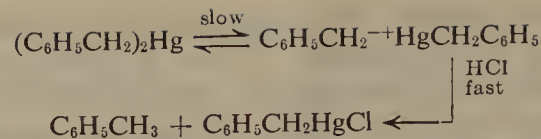*Princeton, New Jersey 08540*
Received July 13, 1967

On the Purported S_E1 Protolysis of Dibenzylmercury

Sir:

Several substitution reactions of organomercurials have been reported to proceed by the S_E1 pathway in which ionization of the C–Hg bond to yield a carbanion is the rate-controlling step.[1-5] What at first appeared to be convincing data was presented by Hart and Ingold[6] for the reaction between di-sec-butylmercury and diethylthallic bromide, but recently Jensen and Heyman[7] have shown that the claim was erroneous and that air oxidation of the mercurial was occurring. As a result of our studies with benzylic mercurials, we were interested in the report of Reutov[8] that HCl protolysis of dibenzylmercury (DBM) in a wide variety of solvents proceeded by the S_E1 mechanism. This reaction has been reinvestigated and we now wish to communicate that carbanions are not involved.

The following is a summary of the observations reported by the Russian workers:[8] (1) the reaction was first order with respect to DBM and zero order with respect to acid in solvents DMSO, DMF, acetonitrile with water contents ranging from 0 to 25 mole%, tetrahydrofuran, and 1-butanol; (2) an increase in the water content of the solvent acetonitrile decreased the reaction rate, although the reaction was still first order over-all; (3) the rate sequence as a function of solvent was CH_3CN (5% H_2O) > n-C_4H_9OH > THF > DMF > DMSO, in which order DMSO has a surprisingly feeble ability, when compared with THF or n-C_4H_9OH, to promote ionization of the C–Hg bond.

The following scheme was considered consistent with these data.

$$(C_6H_5CH_2)_2Hg \underset{}{\overset{slow}{\rightleftharpoons}} C_6H_5CH_2^{-\,+}HgCH_2C_6H_5$$
$$C_6H_5CH_3 + C_6H_5CH_2HgCl \longleftarrow \Big| \overset{HCl}{\underset{fast}{}}$$

A number of aspects of the investigation and interpretation seemed questionable for the following reasons.[9] (1) It seemed strange to us that DBM was apparently stable in aqueous acetonitrile in the absence of acid. Protic capture of the carbanions would be expected to be rapid, and a hydrolytic demercuration should ensue. (2) No products were identified, nor was the function of the atmosphere apparently probed. (3) The kinetics were obtained on reaction mixtures containing equimolar amounts of HCl and DBM. Never were these concentrations varied independently, thus prohibiting full kinetic analysis. No acid, other than HCl, was employed as a proton source. (4) The reaction seemed unreasonably fast when compared with the HCl cleavage in dioxane, reported[10] to proceed by second-order kinetics. That THF and dioxane differed so markedly in their abilities to promote C–Hg bond ionization seemed strange. (5) The effects of solvents on the rates seemed inexplicable on any reasonable grounds, considering the postulated heterolytic pathway. The explanation advanced by the Russian workers is absolutely untenable, since it proposes slight changes in the "effectiveness" of the acid as a result of solvent–acid interactions. It should be clear that the role of acid is postulated to be post rate determining, and hence information on such a step does not follow from the kinetics. (6) As judged by the illustrations of kinetic plots, rarely was the reaction followed for the duration of 1 half-life.

Our studies have shown that the reactions of DBM with HCl yield some toluene (vpc) and benzylmercuric chloride (proton spectrum with the characteristic ^{199}Hg–CH_2 spin coupling). We could detect no significant amounts of dibenzyl in the nmr spectrum. However, studies (via nmr) did indicate a significant departure from the anticipated 1:1 stoichiometry of DBM to $C_6H_5CH_2HgCl$. We established that DBM experienced no reaction in aqueous acetonitrile during 6 hr at 40°, under which conditions the reported half-life for carbanion production was ca. 40 min. This strongly suggests that carbanions are not being generated in this medium.

The kinetics of the reaction between DBM and HCl in aqueous CH_3CN were followed by titration of residual acid. Plotted as first order in DBM, the line showed a very serious drift to faster rates. The data were only poorly reproduced by second-order plots, with a serious rate acceleration after an initial slower period. Other kinetic schemes, designed to allow for possible halide ion participation, did not correlate the data any better. However, the initial slopes of the first-order plots were clearly a function of HCl concentration, although some erratic behavior was encountered. Use of CF_3COOH as a proton source led to a much depressed rate,[11] confirming that carbanion generation was not rate determining. Independent measurements on the rate of cleavage of $C_6H_5CH_2HgCl$ with HCl established that this

(1) O. A. Reutov, V. I. Sokolov, and I. P. Beletskaya, *Dokl. Akad. Nauk SSSR*, **136**, 631 (1961); *Izv. Akad. Nauk SSSR*, 1217 (1961).
(2) O. A. Reutov, B. Praisner, I. P. Beletskaya, and V. I. Sokolov, *ibid.*, 970 (1963).
(3) E. D. Hughes, C. K. Ingold, and R. M. G. Roberts, *J. Chem. Soc.*, 4372 (1964).
(4) I. P. Beletskaya, V. I. Karpov, V. A. Moskalenko, and O. A. Reutov, *Dokl. Akad. Nauk SSSR*, **162**, 86 (1965).
(5) I. P. Beletskaya, V. I. Karpov, and O. A. Reutov, *ibid.*, **161**, 586 (1965).
(6) C. R. Hart and C. K. Ingold, *J. Chem. Soc.*, 4372 (1964).
(7) F. R. Jensen and D. Heyman, *J. Am. Chem. Soc.*, **88**, 3438 (1966).
(8) I. P. Beletskaya, L. A. Fedovov, and O. A. Reutov, *Dokl. Akad. Nauk SSSR*, **163**, 1381 (1965).

(9) The reaction was followed by estimating ionic chloride by a mercurimetric technique (Hg(NO$_3$)$_2$ in acid solution). We could envisage several problems with this procedure.
(10) F. Nerdel and S. Makover, *Naturwissenschaften*, **45**, 490 (1958).
(11) Under comparable conditions CF_3COOH was consumed ca. 10^2 times more slowly than HCl.

consecutive reaction was not significant during the reaction time. Also, deliberate addition of $C_6H_5CH_2$-HgCl at the start of a run had essentially no effect on the rate, eliminating product catalysis as a source of the kinetic disturbance. Addition of HCl to CH_3CN was insignificant under these conditions.

We suspected that atmospheric oxygen was to blame for the situation. This was dramatically confirmed by data from runs conducted under a N_2 atmosphere. The consumption of HCl was now very slow, and virtually no disappearance of HCl occurred during the time when the reaction was previously essentially complete. Toward the end of a run medical air was admitted and the consumption of HCl was enormously accelerated. Clearly we are dealing with an oxygen-promoted reaction and protons, halide, and oxygen apparently form a very effective liason for cleavage of the mercurial.[11a] Under oxygen-free conditions, at 40°, the reaction between DBM and HCl correlates well with second-order kinetics for a satisfactory period before consecutive reactions intervene. The period of induction and erratic

(11a) NOTE ADDED IN PROOF. The rate of reaction under aerobic conditions was at least 10^2 greater than that for the reaction under anaerobic conditions. A referee has kindly drawn our attention to a paper by M. M. Kreevoy and R. L. Hansen (*J. Phys. Chem.*, **65**, 1055 (1961)) who noted that the reactions of isopropyl- and *t*-butylmercuric iodides with perchloric acid were profoundly accelerated by oxygen with rate enhancements of *ca.* 10^2–10^3. Although the details of the aerobic reaction are not clear, oxygen insertion into the C–Hg bond may well be a key step in the sequence. Our chief concern was to demonstrate that the reaction was not of the SE1 type.

behavior under normal atmospheric conditions are the trademarks of radical-chain processes. Reactions between R_2Hg and O_2 are now well documented.[7,12]

This finding, coupled with that of Jensen,[7] has serious implications for other reported SE1 reactions of organomercurials. Thus we are disinclined to accept the report[13] of the "monomolecular protolysis of phenylmercuric bromide in 70% aqueous dioxane," and the reported SE1 protolysis of *trans*-ClCH=CHHgCl in $DMSO^4$ seems unreasonably rapid ($t_{1/2} \sim 9$ min at 20°), considering that such mercurials are prepared and are stable in 6 *N* HCl.[14] The reactions of ClCH=CHHgCl with both I_2[5] and HCl[4] in DMSO are reported to be of the SE1 type, implying identical rates for both reactions. However the iodine cleavage reportedly proceeds more rapidly at 20° ($k_1 = 3.6 \times 10^{-3}$ sec^{-1}) than does the HCl protolysis at 30° ($k_1 = 1.3 \times 10^{-3}$ sec^{-1}), suggesting some irregularity.

(12) See, for example, Yu. A. Aleksandrov, O. N. Druzhkov, S. F. Zhil'tsou, and G. A. Razuvaev, *Dokl. Akad. Nauk SSSR*, **157**, 1395 (1964), and subsequent papers.
(13) I. P. Beletskaya, A. E. Myshkin, and O. A. Reutov, *Izv. Akad. Nauk SSSR, Otd. Khim. Nauk*, **2**, 240 (1965); see also ref 8.
(14) See, for example, A. N. Nesmeyanov and R. Kh. Freidlina, *Bull. Acad. Sci. USSR, Div. Chim. Sci.*, 150 (1945), and subsequent papers.

Brian F. Hegarty, William Kitching, Peter R. Wells
*Department of Chemistry, University of Queensland
Brisbane, Australia*

Additions and Corrections

New Structural and Stereochemical Aspects of the Cyclization of Olefinic Acetals [*J. Am. Chem. Soc.*, **89**, 170 (1967)]. By WILLIAM S. JOHNSON, ARNE VAN DER GEN, and JOHANN J. SWOBODA, Department of Chemistry, Stanford University, Stanford, California 94305.

The following paragraph should be added at the end of the paper.
Acknowledgment. We thank the U. S. Public Health Service, the National Science Foundation, and the donors of the Petroleum Research Fund, administered by the American Chemical Society, for support of this research.

Mechanisms of Photochemical Reactions in Solution. XLIV. Photodimerization of Cyclohexenone [*J. Am. Chem. Soc.*, **89**, 3482 (1967)]. By ERNEST Y. Y. LAM, DONALD VALENTINE, and GEORGE S. HAMMOND, Gates and Crellin Laboratories of Chemistry, California Institute of Technology, Pasadena, California 91109.

On page 3483, column 2, the beginning of line 13 should read: enone concentration is 0.05 *M*.

Mechanisms of Reactions of Thiolsulfinates (Sulfenic Anhydrides). I. The Thiosulfinate–Sulfinic Acid Re-

action [*J. Am. Chem. Soc.*, **89**, 3557 (1967)]. By JOHN L. KICE, CLIFFORD G. VENIER, and LESLIE HEASLEY, Department of Chemistry, Oregon State University, Corvallis, Oregon 97331.

On page 3559, eq 2b should read

$$(ArSO_2H)_{av} = (ArSO_2H)_0 - a(Ib)_0/2 \qquad (2b)$$

The Thiolochromium(III) Ion [*J. Am. Chem. Soc.*, **89**, 3661 (1967)]. By MICHAEL ARDON and HENRY TAUBE, Department of Chemistry, Stanford University, Stanford, California 94305.

On page 3662, column 1, line 13, $Cr(H_2O)_5Cl^{2+}$ should read $Cr(H_2O)_5I^{2+}$.

Steric Hindrance to the Formation of and Protonation of the Nitronate Ion from 2-Aryl-1-nitrocyclohexanes [*J. Am. Chem. Soc.*, **89**, 3906 (1967)]. By F. G. BORDWELL and MARTHA M. VESTLING, Department of Chemistry, Northwestern University, Evanston, Illinois 60201.

On page 3906, column 2, line 18, (axial) should read (equatorial).

Book Reviews

Conformations of Macromolecules. By T. M. BIRSHTEIN and O. B. PTITSYN, Institute of High Molecular Compounds, Leningrad, U.S.S.R. Translated from the Russian Edition by SERGE N. TIMASHEFF and MARINA J. TIMASHEFF. Interscience Publishers, John Wiley and Sons, Inc., 605 Third Ave., New York, N. Y. 1966. xiv + 350 pp. 15.5 × 23.5 cm. $14.50.

The properties of both synthetic and biological polymeric materials depend to a very considerable extent on the arrangement of the linear chain molecules of which they are composed. Each of these chains may be arranged in a great number of possible rotameric (rotational isomeric) states. Fortunately, general methods of analysis of polymer molecules by a rotameric model can be worked out in detail. These depend on two important unifying ideas: (1) the short-range interactions of a polymer may be described by a Markoff process; (2) transitions in polymer molecules, particularly biological polymer molecules, are special examples of a one-dimensional Ising lattice model.

The authors of this small treatise and other colleagues at the Institute for High Molecular Weight Compounds in Leningrad have themselves developed many of the ideas and methods presented here. Their book is primarily an exposition of the theory, in addition, drawing very heavily upon experimental results which bear on the subject. The titles of the chapters describe the subjects covered. These are:

1. Flexibility of Macromolecules and Their Physical Properties
2. Internal Rotation and Rotational Isomerism
3. Conformations of Macromolecules and Mechanism of Their Flexibility
4. Statistics of One-Dimensional Cooperative Systems
5. Theory of the Dimensions and Dipole Moments of Macromolecules: General Methods
6. Theory of the Dimensions and Dipole Moments of Macromolecules: Equations for Real Chains
7. Comparison of the Theory with Experiment and Conformations of Typical Macromolecules in Solution
8. Conformations of Macromolecules and Mechanical Properties of Polymers
9. Theory of Conformational Transitions in Polypeptide Chains
10. Effect of External Factors on Conformational Transitions in Polypeptide Chains
11. Theory of Conformational Transitions in Polynucleotide Chains

This book is exceptionally well done, the exposition is clear, the nature of the assumptions is directly stated, and the mathematical arguments are given in detail. The list of references seems to be complete including papers published as late as 1964.

For scientists who plan research in the statistics of polymer chains, this book is a godsend and a welcome substitute for an extensive study of the literature. For experimental workers who will be using the results of the rotameric theory of polymer chains or the results of the theory of polypeptide and polynucleotide transitions, the most direct and clear source of the analysis of the problem will also be found in this book. Graduate students will find it, alas, very expensive, though of primary importance if they plan investigations in this subject.

This excellent work extends and amplifies the earlier treatise "Configurational Statistics of Polymer Chains" by M. V. Volkenstein, a colleague of the present authors at the Institute in Leningrad.

Robert Ullman

Chemistry Department, Scientific Laboratory
Ford Motor Company, Dearborn, Michigan 48121

Polymerization by Organometallic Compounds. By LEO REICH, Picatinny Arsenal, Dover, N. J., and A. SCHINDLER, Camille Dreyfus Laboratory, Research Triangle Institute, Durham, N. C. Interscience Publishers, John Wiley and Sons, Inc., 605 Third Ave., New York, N. Y. 1966. x + 740 pp. 16 × 23.5 cm. $25.00.

In all fairness a book should be judged by how close it comes to fulfilling the stated purposes of the author, even though it be bought for its ultimate utility.

According to the preface "A major objective of this book is to present, ... in an organized and categorized sequence, pertinent information derived from the literature ... on organometallic polymerizations. This book should be useful mainly to research workers and graduate students who have already been introduced to polymer chemistry and who desire to broaden their knowledge in the field of organometallic catalyzed polymerizations. This book is by no means directed toward a specialist in this field nor is it intended as a reference work." The authors have tried hard to meet these goals, but the book has several major faults in the eyes of this reviewer. The book reads as if the authors summarized a paper in a given field, picked up the next one and summarized it, and so on to the bottom of the pile. No attempt was made to collate the information, to analyze it, or to introduce any critical judgement about divergent "facts" or opinions. Having worked with organometallic catalysts, this reviewer is well aware of the difficulty of separating "facts from artifacts" in this field. If the book had been written for experts, a case could be made for including all references (the book does not) without comment, but when it is ostensibly written for the nonexpert, this approach is indefensible.

The second objection is a more practical one, and is related to the arrangement in the book. Broadly speaking, the authors chose to organize the book according to the organometallic part of the title and not the polymerization part. So one cannot open the book to read about the polymerization of butadiene, or isoprene, or methyl methacrylate, without frequent referral to the index. As a result, the nonexpert is bound to come away with the feeling that there is no mechanistic difference between the polymerization of an olefin and a diene with a Ziegler catalyst. He will read 150 pages on the importance of the nature of the surface of a Ziegler–Natta catalyst before he is told on p 266 that there are soluble catalysts for the polymerization of ethylene; this is not as bad as it sounds because the authors describe the Cp_2TiCl_2 catalysts as being very unreactive (they are actually among the most active catalysts known). He will read an excellent discussion on the base-catalyzed polymerization of styrene and α-methylstyrene, but will only discover that methyl methacrylate can be polymerized similarly when the authors wish to discuss termination, which they cannot do very well with the "living polymers."

The book is not limited to a discussion of Ziegler–Natta catalysis. The authors use the usual definition of organometallic (containing a carbon–metal bond); for purposes of inclusion, however, they ignore any mechanistic implications and require simply that such a bond be present initially in the catalyst. The extent of coverage is best gleaned from the table of contents: I. Historical Development (6 pp); II. General Theoretical Concepts of Polymerization (108 pp); III. Some General Considerations on Catalyst Activity (128 pp); IV. Mechanism and Kinetics of Polymerizations with Ziegler–Natta Type Catalyst Systems (159 pp); V. Alfin Catalysts (29 pp); VI. Metaloorganic Catalyst Systems Involving Free Radical Mechanisms (61 pp); VII. Anionic Polymerization (177 pp); VIII. Some Aspects of Cationic Polymerization (11 pp); IX. Copolymerization (27 pp). The second chapter is a hodgepodge of information, which serves mostly to outline the authors' interests; the reader would do better to read Billmeyer and Flory. The last chapter, in view of the recent apperance of an excellent monograph on the subject, could also have been omitted.

In summary, nonexperts will obtain an introduction of sorts to this fascinating area of polymer science by reading this book, and people who are knowledgeable in the field are bound to find interesting tidbits which they have missed in their own reading. But the scientific world has long awaited a definitive book on polymerization by organometallic catalysts, and I regret to say that the wait is not over.

David S. Breslow

Research Center, Hercules Incorporated
Wilmington, Delaware 19899
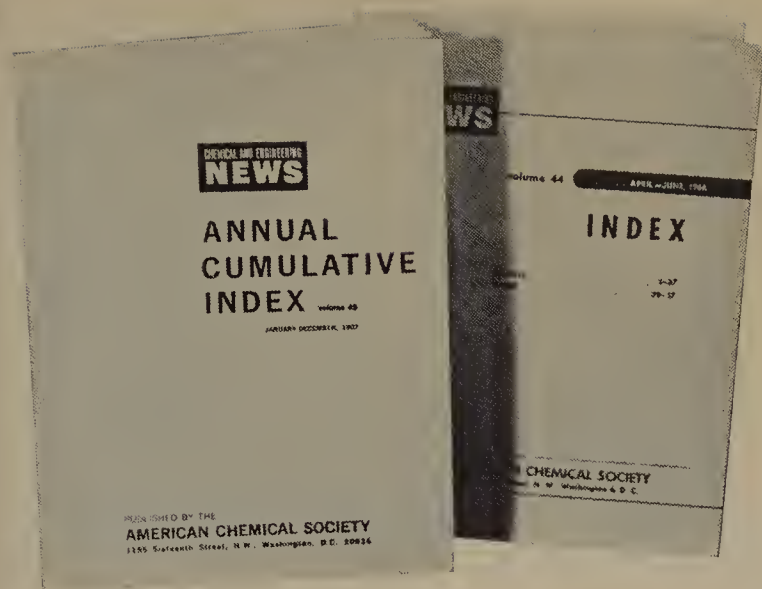
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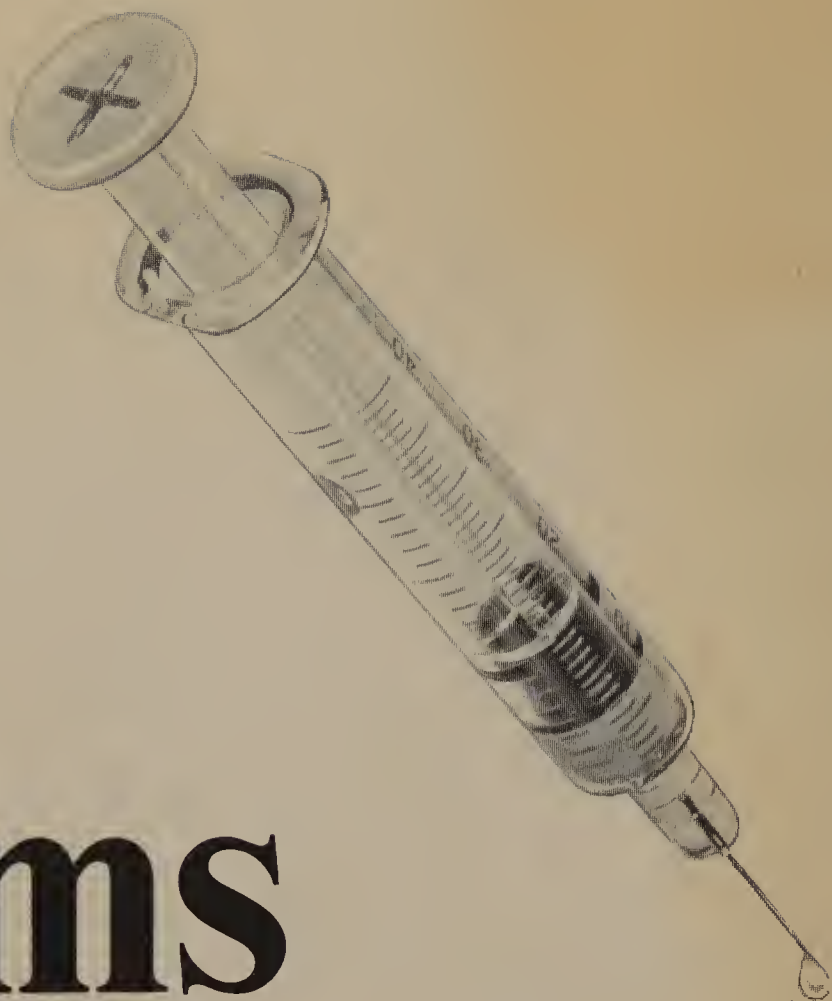_____ **Four Quarterlies + Annual Cumulative.** Price $20.00 Postpaid.

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